University of Pisa
Degree course in Mathematics

MASTER'S DEGREE THESIS

The key role played by the Public Health System on the vaccination programs and the eradication of children's infectious diseases

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A mio cugino Paolo.

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Introduction

0.1 Modeling the interplay between human behavior and the spread of infectious diseases

Infectious diseases are those illnesses caused by an infecting organism (virus, bacterium, fungal pathogen, protozoa or parasite) that can be spread between individuals.
Modern infectious disease epidemiology, that is the branch of medicine dealing with the study of the causes, distribution and control of infectious diseases, has a strong history of using mathematics both for prediction and to achieve a deeper understanding.
The current mathematical theory of infectious disease transmission was built on a few cornerstone ideas and models developed during the so-called Golden Age of theoretical ecology ($1923 - 1940$). The most important among such milestones is the homogeneous mixing SIR (susceptible-infective-recovered) model in its two variations, for epidemic outbreaks, as seasonal influenza, and for endemic infections, as measles, in large communities in absence of any immunization.
In the last 30 years however, thanks to pioneering works aiming to better integrate models with data, mathematical models of infectious diseases have crossed their traditional biomathematical boundaries to become central supporting tools for public health decisions and policies, such as determining the duration of travel restrictions or of school closure during a pandemic event, or the fraction of newborn to be immunized for a vaccine-preventable infection, as measles. A major example is provided by the huge advancements in the modeling and prediction in relation to the pandemic threats, from the avian flu scare, to the SARS outbreaks, to the H1N1 influenza pandemic that scared the world in 2009.
Despite these advancements in this sophisticated modeling behavioral, influences are not considered.

It is exactly here that the discipline of behavioral epidemiology (BE) of infectious diseases emerges. It is a new branch of infectious disease epidemiology focusing on the complex interplay between human behavior and its determinants (such as acquisition of information, risk perception, perceived benefits and costs of different actions) and the transmission and control of infectious diseases.

0.2 Immunization programs and behavioral epidemiology

We finally know something about social contact patterns. But what we know mostly deals with social behavior in "normal life" days, therefore in absence of illness, of serious life-threatening conditions, and so on. How might people socially respond in the presence of a big, real, pandemic threat, and how these individual responses might impact on transmission and control, we simply do not know. But there are other areas, beyond pandemic threats, where human behavior is becoming a critical determinant of infectious diseases dynamics, first of all the area of immunization choices.

The history of immunization in the western world has always been characterized, already since the introduction of smallpox vaccine, by phases of declining uptake. However, most of this historical opposition to vaccination is thought to be due to conscientious, religious or philosophical reasons.

In contrast, current industrialized societies are gradually facing the more complex challenge of "rational" opposition to vaccines. Consider the example of an infection that is preventable by childhood immunization, as measles, for which we assume there are only two options: vaccinating or not vaccinating at birth. In several countries the increasing coverage with MMR (Measles-Mumps-Rubella), within the WHO (World Health Organization) plan for global measles elimination, has driven circulation of the disease to minimal levels or even zero incidence. As incidence of the disease goes on to decline thanks to vaccination, families become increasingly concerned with the risks associated with vaccines. If families start perceiving that the chance of acquiring infection for their children is lower compared to the risk of experiencing damages from the vaccine, they could believe it rational not to vaccinate their children, particularly if they perceive that the rest of the population will, instead, vaccinate (example of "free-riding" behavior).

European data suggest that sanitation progress and mass immunization, two major factors underlying the changed relation between humans and their diseases, are now acting as "killers" of the perceived rewards of immunization.

Immunization against an infectious disease by a preventable vaccine has a twofold protective effect: a direct one for those who are immunized and an indirect one for those who are not, due to the reduced circulation of the pathogen in the community which reduces the risk of acquiring infection for those non-immunized. Consequently, as already seen above, free-riding arises: some individuals take advantage of this indirect protection (herd immunity) created by those who choose to be vaccinated, in order to avoid immunization and its related costs.

Therefore, we can understand why we can claim that it is the vaccine's success itself in controlling infections that promotes "rational" opposition: vaccine's success can lead to declining vaccine coverage and, consequently, to an increase in susceptibility which is related to the risk of infectious disease resurgence.

The modeling of vaccination choices and "rational" opposition is currently a major topic of investigation in BE.

0.3 Immunization trend against measles in Italy between years 1996 and 2008

As an example, but also as subject of study of this thesis, let us report here concrete values of vaccine uptake (against measles) observed in an industrialized country (Italy) in a certain period of time (in $1996 - 2008$ years).

In 1996, the MMR coverages ranged between 25% and 80%, with a national average of 56%. This dramatically low measles coverage, compared to the WHO target (95% first dose), made measles immunization one of the priorities of the Public Health System (PHS). The main actions taken were (a) the development, as from 1998 of a new nationwide immunization schedule unifying all pediatric immunizations, without distinction between compulsory and recommended ones, (b) the free offer of MMR at the age of 12 months with other immunizations, (c) approval in 2003 of the National Plan for Measles and Congenital Rubella Elimination, allocating of resources for further increasing first dose coverage and for a national campaign targeting school-age children. Such measures allowed the first dose national coverage to increase up to 78% in 2003, and then to 90% in 2008, with some regions above the WHO target, and with a marked decline in geographic inhomogeneity. These suggest that the recent public health subsidies have put an end to the stagnation due to the long-standing voluntariness of the Italian MMR program.

0.4 Structure and purposes of my thesis

This thesis focuses on epidemiological models able to describe the spread of a pediatric infectious disease (such as measles) that could be controlled by immunization (mandatory or voluntary) with a 100% effective vaccine administered in a single dose at birth and giving life-long immunity.
Firstly, the well-known basic $SIR - model$ is introduced in two different variations, that are $SIR - model$ with no immunization and with mandatory vaccination. Even if the second version gives instructions on how achieve disease eradication under proper high levels of mandatory vaccination, both of them exhibit a limit in not considering the relationship between human behavior and vaccination programs. Therefore, subsequently, two variations of basic $SIR - models$, that on the contrary are able also to account for it, are presented and analysed.
When the incidence and prevalence of most common vaccine preventable childhood infectious diseases are constantly low, as is the case in many industrialized countries, the incidence of vaccine-associated side effects might become a key determinant in vaccine assumption. This leads to analyse a SIR transmission model with voluntary vaccination, in which dynamic demand is based on an imitation mechanism where the perceived risk of vaccination is modelled as a function of the incidence of vaccine side effects.
Finally, inspired by the considerable increase in routine measles vaccine uptake recently (between 1996 and 2008 years) observed in Italy after a set of public interventions, another SIR trasmission model with voluntary vaccination is proposed. In this new and last model, vaccinating behavior spreads not only through the diffusion of private information spontaneously circulating among parents of children to be vaccinated, as it happens in the previous model, but also through public information communicated by the public health autorities.
The purpose of the thesis is to show how this latter model underlines the importance of Public Health System (PHS) intervention in order to avoid dramatic drops in vaccine uptake for children's infectious diseases considered not "circulating" (as it happens in industrialized countries thanks to years of effective immunization) and in order to achieve disease eradication. In particular, PHS is shown to play a stabilising role, in the sense that it is able to reduce the strength of imitation-induced oscillations in vaccine uptake and to maintain vaccination always at some positive, and usually rather high, values.
It can be proved that PHS not only allows disease elimination, but it even makes the Disease-Free Equilibrium where everyone is vaccinated globally attractive.

Finally, the thesis also illustrates how this last model seems to provide a much more plausible behavioral explanation of the increase in vaccine uptake against measles, observed in Italy between 1996 and 2008 years, than models based on imitation alone.

Setting and notations

The population under consideration is divided into three disjoint classes: the susceptible class consists of those individuals who can incur the disease but are not yet infective; the infective class consists of those who are transmitting the disease to others; the removed class consists of those who are removed from the susceptible-infective interaction by recovery with immunity or isolation. The fractions of the total population in these classes are denoted by $S(t), I(t)$ and $R(t)$, respectively (from this comes the sigla SIR).
Over time a portion of the population moves from class to class.
The following assumptions are made:

- The population is uniform, homogeneously mixing and considered of constant size 1. Therefore, the above three different classes are related by equation
$$S(t) + I(t) + R(t) = 1. \tag{1}$$

- Births and deaths occur at equal rates and all newborns are susceptible. Individuals are removed by death from each class at a rate proportional to the class size with proportionality constant μ, which is called the daily death removal rate. Therefore, $1/\mu$ is the average lifetime.

- The daily contact rate β is the average number of contacts per infective per day; it is fixed and it does not vary seasonally. A contact of an infective is an interaction which results in infection of the other individual if he is susceptible. Thus the average number of susceptibles infected by the infective class per day is βSI.

- Individuals recover and are removed from the infective class at a rate proportional to the number of infectives with proportionality constant ν. Therefore, $1/\nu$ is the average duration of disease.

- $R_0 := \frac{\beta}{\mu+\nu}$ is the Basic Reproduction Number, representing the average number of contacts (with both susceptibles and others) of an infective during his infectious period.

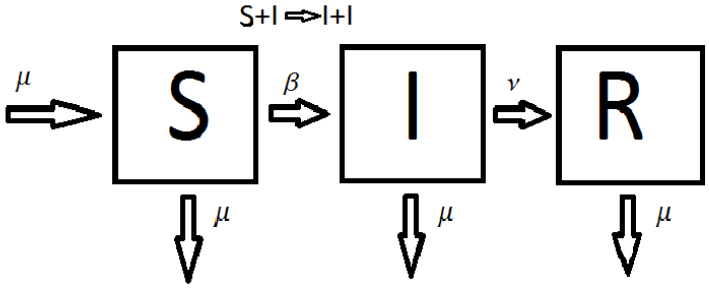

Figure 1: Compartmental caricature of the basic $SIR-model$ with no immunization. The arrows between boxes show transition or movement between classes; arrows entering or leaving the system correspond to births and deaths respectively.

- $Re(t) := R_0 S(t)$ is the Effective Reproduction Number.
- The initials DFE stay for Disease-Free Equilibrium, EE for Endemic Equilibrium, LAS for Locally Asymptotically Stable and GAS for Globally Asymptotically Stable.

Basic SIR-models and their intrinsic limitations

0.5 The model: SIR-model with no immunization

Firstly, let us consider the basic $SIR-model$ with no immunization.
According to the chapter of setting and notations (in particular see figure (1)), the corresponding model can be written as

$$\begin{cases} S' = \mu - \mu S - \beta SI \\ I' = \beta SI - (\mu + \nu)I \\ R' = \nu I - \mu R. \end{cases}$$

But since relation (1) links the state variables $S(t), I(t)$ and $R(t)$, the dynamics of $R(t)$ can be inferred once we know that ones of $S(t)$ and $I(t)$. Therefore, the system above reduces to

$$\begin{cases} S' = \mu - \mu S - \beta SI \\ I' = \beta SI - (\mu + \nu)I. \end{cases} \tag{2}$$

0.6 Equilibria

Let us find the equilibrium points of system (2) putting the derivatives of the state variables $S(t)$ and $I(t)$ equal to zero, that is to say

$$\begin{cases} S' = \mu - \mu S - \beta SI = 0 \\ I' = \beta SI - (\mu + \nu)I = 0. \end{cases}$$

Looking at the second equation: $I' = \beta SI - (\mu + \nu)I = \beta I(S - R_0^{-1}) = 0$, we infer that we should have $I = 0$ or, if $R_0 > 1$, $S = R_0^{-1}$.

- If $I = 0$, from the first equation we obtain $S = 1$ and therefore we have the DFE point $A_1 = (1, 0)$ where everybody is susceptible and nobody is infective.
- If $I \neq 0$, it should be $S = R_0^{-1}$ and so from the first equation we have $\mu - \mu R_0^{-1} - (\mu+\nu)I = 0$, that implies $I = \frac{\mu(1-R_0^{-1})}{\mu+\nu}$. Consequently, there exists also an EE point $A_2 = \left(R_0^{-1}, \frac{\mu(1-R_0^{-1})}{\mu+\nu}\right)$ if and only if $R_0 > 1$.

Now, let us look at the local stability of these equilibria considering the Jacobian matrix associated to system (2):

$$J = \begin{pmatrix} \frac{\partial S'}{\partial S} & \frac{\partial S'}{\partial I} \\ \frac{\partial I'}{\partial S} & \frac{\partial I'}{\partial I} \end{pmatrix} = \begin{pmatrix} -\mu - \beta I & -\beta S \\ \beta I & \beta S - (\mu + \nu) \end{pmatrix}.$$

0.6.1 Stability of the DFE A_1

The Jacobian matrix at $A_1 = (1, 0)$ is:

$$J_{|A_1} = \begin{pmatrix} -\mu & -\beta \\ 0 & \beta - (\mu + \nu) \end{pmatrix},$$

and the corresponding characteristic polynomial:

$$det(J_{|A_1} - \lambda Id) = \lambda^2 + (\mu - \beta + (\mu + \nu))\lambda - \mu(\beta - (\mu + \nu)) = 0.$$

From the equation above, we can find the following eigenvalues:

$$\lambda_1 = -\mu < 0, \quad \lambda_2 = \beta(1 - R_0^{-1}).$$

Consequently, if $R_0 < 1$, also λ_2 is negative, therefore A_1 is LAS and we reach a state in which everybody is susceptible and nobody infective.
On the contrary, if $\underline{R_0 > 1}$, $\underline{A_1}$ is $\underline{unstable}$.

Actually, we can show that, if $\underline{R_0 < 1}$, $\underline{A_1}$ is $\underline{GAS}$:

Proof. Since $S \leq 1$, we have

$$I' = \beta SI - (\mu + \nu)I = \beta I(S - R_0^{-1}) \leq \beta I(1 - R_0^{-1}).$$

Let us now search the general solution $I_*(t)$ of the differential equation

$$I' := \beta I(1 - R_0^{-1}),$$

defined by the right hand side of the inequality above.

Integrating both sides of $\frac{dI}{I} = \beta(1-R_0^{-1})dt$, we can find the following general solution

$$I_*(t) = C\exp(\beta(1-R_0^{-1})t),$$

with C a positive constant.
Therefore, since $R_0 < 1$, $\beta(1-R_0^{-1}) < 0$, and so

$$\lim_{t\to\infty} I_*(t) = 0.$$

Consequently, using comparison properties for differential equations (see theorem 7 of chapter 1 of book [11]),

$$0 \leq \liminf_{t\to\infty} I(t) \leq \limsup_{t\to\infty} I(t) \leq \lim_{t\to\infty} I_*(t) = 0$$

and so

$$\lim_{t\to\infty} I(t) = 0.$$

If we read now the equation $S' = \mu - \mu S - \beta SI$ for long time, we have $S' \longrightarrow \mu(1-S)$ for $t \to \infty$.
Integrating the differential equation defined by $S' := \mu(1-S)$, we can find that it admits as general solution

$$1 - \tilde{C}\exp(-\mu t),$$

with $\tilde{C}$ a positive constant.
Therefore,

$$\lim_{t\to\infty} S(t) = \lim_{t\to\infty}(1-\tilde{C}\exp(-\mu t)) = 1.$$

In conclusion, we have shown that, if $R_0 < 1$,

$$\lim_{t\to\infty}(S(t), I(t)) = (1,0) = A_1,$$

which means A_1 is GAS. □

0.6.2 Stability of the EE A_2

For the existence condition on A_2, we assume now to be in the case of $\underline{R_0 > 1}$.
Furthermore, let us define the Critical Elimination Coverage p_c as
$p_c := 1 - R_0^{-1}$, whose meaning will be understood later on.
The Jacobian matrix at $A_2 = \left(R_0^{-1}, \frac{\mu(1-R_0^{-1})}{\mu+\nu}\right) = \left(R_0^{-1}, \frac{\mu p_c}{\mu+\nu}\right)$ is:

$$J_{|A_2} = \begin{pmatrix} -\mu R_0 & -(\mu+\nu) \\ \mu(R_0-1) & 0 \end{pmatrix},$$

and the corresponding characteristic polynomial:

$$det(J_{|A_2} - \lambda Id) = \lambda^2 + \mu R_0 \lambda + \mu(\mu + \nu)(R_0 - 1) = 0.$$

From the equation above, we can find the following eigenvalues:

$$\lambda_{1,2} = \frac{-\mu R_0 \mp \sqrt{\mu^2 R_0^2 - 4\mu(\mu + \nu)(R_0 - 1)}}{2},$$

Consequently, since $R_0 > 1$, in both cases of real or complex eigenvalues, λ_1 and λ_2 have negative real part and therefore A_2 is LAS.
Now, we can observe that A_2 is in the interior of the definition set of the state variables $(S(t), I(t))$, that is the triangle $T := \left\{(S, I) \in \mathbb{R}^2_+ / S + I \leq 1\right\}$. The Bendixon-Dulac test (see theorem 3.1 of article [5]), with multiplying factor $\frac{1}{I}$, leads to

$$\frac{\partial}{\partial S}\left(\frac{\mu}{I} - \frac{\mu S}{I} - \beta S\right) + \frac{\partial}{\partial I}\left(\beta S - \mu - \nu\right) = -\frac{\mu}{I} - \beta < I,$$

so that there are no limit cycles or cycle graphs in T.
Furthermore, the only path in T approaching the saddle equilibrium A_1 is the $S-$axis (its one dimensional stable manifold).
Thus, all paths in T except the $S-$axis approach A_2.
Therefore, $\underline{A_2}$ is $\underline{GAS}$.

0.6.3 Equilibria and their stability: summary

- If $\underline{R_0 < 1}$, there is only the DFE $\underline{A_1 = (1, 0)}$ that is $\underline{GAS}$;
- if $\underline{R_0 > 1}$, $\underline{A_1}$ becomes $\underline{unstable}$ and it appears the EE $\underline{A_2 = \left(R_0^{-1}, \frac{\mu p_c}{\mu + \nu}\right)}$, which is $\underline{GAS}$ (with the only exception of the $S-$axis).

Note that if there is no immunization, it is unlikely to have the DFE A_1; therefore, since now on, we assume $R_0 > 1$, that means in absence of vaccination the disease is endemic.

0.7 The model: SIR-model with mandatory vaccination

We can try and control endemic SIR diseases through mandatory vaccination, that allows us to achieve a costant vaccine uptake p_{SIR}.

The corresponding model can be written as

$$\begin{cases} S' = \mu(1 - p_{SIR}) - \mu S - \beta SI \\ I' = \beta SI - (\mu + \nu)I \\ R' = \nu I - \mu R, \end{cases}$$

which reduces, thanks to relation (1), to

$$\begin{cases} S' = \mu(1 - p_{SIR}) - \mu S - \beta SI \\ I' = \beta SI - (\mu + \nu)I. \end{cases} \tag{3}$$

0.7.1 Equilibria and their stability: summary

As we can see this model is close to the previous one. But here the rate μ at which new susceptibles are generated is reduced to $\mu(1 - p_{SIR})$ and the role played by the Critical Elimination Coverage p_c is replaced by $p_c - p_{SIR}$. Consequently, through easy passages similar to those of the previous section, we can find the following summary:

- if $\underline{p_c < p_{SIR}}$, there is only the DFE point $\underline{B_1 = (1 - p_{SIR}, 0)}$ that is $\underline{GAS}$;
- if $\underline{p_c > p_{SIR}}$, $\underline{B_1}$ becomes $\underline{unstable}$ and it appears the EE point $\underline{B_2 = \left(R_0^{-1}, \frac{\mu}{\mu+\nu}(p_c - p_{SIR})\right)}$, which is $\underline{GAS}$ (with the only exception of the $S-$axis).

Note that if the constant vaccine uptake p_{SIR} is set to a value higher than p_c, through mandatory immunization we can achieve disease elimination. The condition $p_c < p_{SIR}$ is called May-Anderson Eradication Condition and it explains the epithet Critical Elimination Coverage associated to p_c.

0.8 Intrinsic limitations of basic SIR-models

We can notice that models above are inspired to chemistry: humans are approximated as molecules in a chemical reaction into a well-stirred tank! Indeed, let us see how we can translate basic $SIR - models$ into particles-based models:

- The creation of a new infective from the collision between a susceptible and an already infective is governed by the Law of Mass Action (the

rate of any chemical reaction is proportional to the product of the concentrations of the reagents):

$$S + I \xrightarrow{\beta} I + I; \quad S' = \cdots - \cdots - \beta SI, \quad I' = \beta SI - \cdots .$$

- Influx rate of species S: μ.
- Outflux rate of species S: μp_{SIR}.
- Spontaneous decay of species S: $S \xrightarrow{\mu} 0$.
- Spontaneous decay of species I: $I \xrightarrow{\mu} 0$.
- Transformation of species I into species R: $I \xrightarrow{\nu} R$.

This way of modeling usually works when we deal with a population of big size.
But, in reality, human beings are NOT passive particles! They are active particles endowed with a "psychology".
This is why we are interested in variations of basic $SIR-models$ that, even if they still follow the Law of Mass Action, are able to improve previous models in the direction of taking into consideration also the relationship between human behavior and the dynamics of vaccine uptake.

The impact of vaccine side effects on the natural history of immunization programs: an imitation-game approach

0.9 The model: I-model

We focus now on the impact of Vaccine Side Effects ($VSEs$) on the dynamics of immunization programs for children's infectious diseases, using a SIR trasmission model with voluntary vaccination.
Immunization choices are described by an evolutionary game approach, where the fraction of vaccinated newborn, indicated with the state variable $p(t)$, is determined by an imitation process between agents (parents of children to be vaccinated) who are divided into "vaccinators" and "non-vaccinators".
The corresponding model can be written as:

$$\begin{cases} S' = \mu(1-p) - \mu S - \beta SI \\ I' = \beta SI - (\mu + \nu)I \\ p' = k\Delta E p(1-p). \end{cases}$$

The first two equations are strictly related to those reported in system (3). But now vaccination is not mandatory anymore.
So let us analyse with more details the dynamics of the vaccine uptake:

$$p' = k\Delta E p(1-p).$$

As we can see from this equation, $p(t)$ obeys a learning imitation process where k is the "imitation" coefficient and $\Delta E(t)$ is the perceived pay-off gain of vaccination, which governs switches between the decisions to vaccinate or not to vaccinate.
$\Delta E(t)$ can be defined by the difference between the perceived cost $-\rho_V(t)$ of suffering $VSEs$, as consequence of vaccination, and the perceived cost $-\rho_I(t)$

of suffering serious diseases, as a consequence of infection:

$$\Delta E(t) = -\rho_V(t) + \rho_I(t).$$

Furthermore, we can make the following assumptions:

- $\rho_I(t) = r(I(t))$, with r an increasing function of infective prevalence I and $r(0) \geq 0$ (the larger the spread of infection and the larger the perceived risk of suffering serious diseases);
- $\rho_V(t) = s(p(t))$, with s an increasing function of vaccinated proportion p and $s(0) \geq 0$ (the larger the fraction of vaccinated newborn and the larger the perceived risk of suffering $VSEs$).

Therefore, we can rewrite the more general system above as

$$\begin{cases} S' = \mu(1-p) - \mu S - \beta SI \\ I' = \beta SI - (\mu + \nu)I \\ p' = kp(1-p)(r(I) - s(p)). \end{cases}$$

For the sake of simplicity and in order to do appropriate simulations, let us simplify the assumptions above as it follows:

- $r(I)$ is set to be proportional to the infective prevalence, that is to say $r(I) = \theta I$, with θ a positive constant;
- $s(p)$ is set to be proportional to the vaccinated proportion, that is to say $s(p) = \alpha p$, with α a positive constant.

Consequently, the resulting Imitation-based model ($I - model$) is:

$$\begin{cases} S' = \mu(1-p) - \mu S - \beta SI \\ I' = \beta SI - (\mu + \nu)I \\ p' = kp(1-p)(\theta I - \alpha p). \end{cases} \tag{4}$$

0.10 Equilibria

We can find equilibrium points of system (4) from setting the derivatives of the state variables equal to zero:

$$\begin{cases} S' = \mu(1-p) - \mu S - \beta SI = 0 \\ I' = \beta SI - (\mu + \nu)I = 0 \\ p' = kp(1-p)(\theta I - \alpha p) = 0. \end{cases}$$

Let us start looking at the values of S, I, p that satisfy the second equation $I' = \beta SI - (\mu + \nu)I = 0$, that is to say $I = 0$ or $S = R_0^{-1}$.

- If $I = 0$, then the equations reduces to

$$\begin{cases} S' = \mu(1-p) - \mu S = 0 \\ I = 0 \\ p' = -\alpha k p^2(1-p) = 0. \end{cases}$$

Therefore, from the first equation we infer that $S = 1 - p$ and from the third one that $p = 0$ or $p = 1$.
If $p = 0 \Longrightarrow S = 1 \Longrightarrow$ we find the pre-vaccination DFE point $C_1 = (1, 0, 0)$ (remember equilibria of the basic $SIR - model$ with no immunization).
If $p = 1 \Longrightarrow S = 0 \Longrightarrow$ we find the pure-vaccinator DFE point $C_2 = (0, 0, 1)$.

- If $I \neq 0$, then $S = R_0^{-1}$ and the equations become:

$$\begin{cases} S' = \mu(1-p) - \mu R_0^{-1} - (\mu + \nu)I = 0 \\ S = R_0^{-1} \\ p' = kp(1-p)(\theta I - \alpha p) = 0. \end{cases}$$

From the third equation we infer that $p = 0$ or $p = 1$ or $p = \frac{\theta}{\alpha} I$.
If $p = 1 \Longrightarrow I = -\frac{\mu}{\beta} < 0 \Longrightarrow$ no new equilibria are generated.
If $p = 0 \Longrightarrow I = \frac{\mu}{\mu+\nu}(1 - R_0^{-1}) \Longrightarrow$ we find the pre-vaccination EE point $C_3 = \left(R_0^{-1}, \frac{\mu p_c}{\mu+\nu}, 0\right)$ (remember equilibria of the basic $SIR - model$ with no immunization).
If $p = \frac{\theta}{\alpha} I \Longrightarrow I = \frac{1 - R_0^{-1}}{1 + \frac{\nu}{\mu} + \frac{\theta}{\alpha}} \Longrightarrow$ we find the EE point with positive vaccine uptake $C_4 = \left(R_0^{-1}, \frac{p_c}{1+\frac{\nu}{\mu}+\frac{\theta}{\alpha}}, \frac{\theta}{\alpha}\frac{p_c}{1+\frac{\nu}{\mu}+\frac{\theta}{\alpha}}\right)$.
Note that both equilibria C_3 and C_4 are well defined, since their components are obviously included between 0 and 1.

Now, let us compute the Jacobian matrix associated to system (4) in order to analyse the local stability of equilibria:

$$J = \begin{pmatrix} \frac{\partial S'}{\partial S} & \frac{\partial S'}{\partial I} & \frac{\partial S'}{\partial p} \\ \frac{\partial I'}{\partial S} & \frac{\partial I'}{\partial I} & \frac{\partial I'}{\partial p} \\ \frac{\partial p'}{\partial S} & \frac{\partial p'}{\partial I} & \frac{\partial p'}{\partial p} \end{pmatrix} = \begin{pmatrix} -\mu - \beta I & -\beta S & -\mu \\ \beta I & \beta S - (\mu + \nu) & 0 \\ 0 & k\theta p(1-p) & \frac{\partial p'}{\partial p} \end{pmatrix},$$

where

$$\frac{\partial p'}{\partial p} = -kp(\theta I - \alpha p) + k(1-p)(\theta I - 2\alpha p).$$

0.10.1 Stability of the pre-vaccination DFE C_1

The Jacobian matrix at $C_1 = (1, 0, 0)$ is

$$J_{|C_1} = \begin{pmatrix} -\mu & -\beta & -\mu \\ 0 & \beta - (\mu + \nu) & 0 \\ 0 & 0 & 0 \end{pmatrix}.$$

The linearized equation for I at C_1 reads

$$i' = [\beta - (\mu + \nu)]\, i = \beta(1 - R_0^{-1})i.$$

Therefore, since $R_0 > 1$, $\underline{C_1}$ is always $\underline{unstable}$.

0.10.2 Stability of the pure-vaccinator DFE C_2

The Jacobian matrix at $C_2 = (0, 0, 1)$ is

$$J_{|C_2} = \begin{pmatrix} -\mu & 0 & -\mu \\ 0 & -(\mu + \nu) & 0 \\ 0 & 0 & k\alpha \end{pmatrix}.$$

The linearized equation for p at C_2 reads $\eta' = k\alpha\eta$.
Therefore, since $k\alpha > 0$, $\underline{C_2}$ is always $\underline{unstable}$ too.

0.10.3 Stability of the pre-vaccination EE C_3

The Jacobian matrix at $C_3 = \left(R_0^{-1}, \frac{\mu p_c}{\mu+\nu}, 0\right)$ is

$$J_{|C_3} = \begin{pmatrix} -\mu R_0 & -(\mu + \nu) & -\mu \\ \mu(R_0 - 1) & 0 & 0 \\ 0 & 0 & \frac{\mu k\theta}{\beta}(R_0 - 1) \end{pmatrix}.$$

The linearized equation for p at C_3 reads $\phi' = \frac{\mu k\theta}{\beta}(R_0 - 1)\phi$.
Therefore, since $\frac{\mu k\theta}{\beta}(R_0 - 1) > 0$, also $\underline{C_3}$ is always $\underline{unstable}$.

0.10.4 Stability of the EE C_4 and oscillatority of the system

Let us put $I_4 := \frac{p_c}{1+\frac{\nu}{\mu}+\frac{\theta}{\alpha}}$, therefore $C_4 = (R_0^{-1}, I_4, \frac{\theta}{\alpha}I_4)$.
The study of the stability of this equilibrium can be summarized by the following theorem:

Theorem 0.1 (Stability of the EE C_4)**.**
(A) If

$$\mu\theta\beta I_4 < \alpha(\mu+\beta I_4)(\mu+\beta I_4+2\sqrt{\beta I_4(\mu+\nu)}),$$

then $\underline{C_4}$ is $\underline{LAS}$, irrespective of the imitation speed k.
(B) If

$$\mu\theta\beta I_4 > \alpha(\mu+\beta I_4)(\mu+\beta I_4+2\sqrt{\beta I_4(\mu+\nu)}),$$

then two values $k_1,\ k_2$, with $0<k_1<k_2$, exist such that

1. if $\underline{k\in(0,k_1)\cup(k_2,\infty)}$, then $\underline{C_4}$ is $\underline{LAS}$,

2. if $\underline{k\in(k_1,k_2)}$, then $\underline{C_4}$ is $\underline{unstable}$ and the system is oscillatory in the sense of Yakubovich.

Proof. The Jacobian matrix at C_4 is:

$$J_{|C_4}=\begin{pmatrix} -\mu-\beta I_4 & -(\mu+\nu) & -\mu \\ \beta I_4 & 0 & 0 \\ 0 & k\frac{\theta^2}{\alpha}I_4\left(1-\frac{\theta}{\alpha}I_4\right) & -k\theta I_4\left(1-\frac{\theta}{\alpha}I_4\right)\end{pmatrix},$$

and the corresponding characteristic polynomial is:

$$\begin{aligned} - \quad & det(J_{|C_4}-\lambda Id)=\lambda^3+\left[\mu+\beta I_4+k\theta I_4\left(1-\frac{\theta}{\alpha}I_4\right)\right]\lambda^2+ \\ + \quad & \left[k\theta(\mu+\beta I_4)I_4\left(1-\frac{\theta}{\alpha}I_4\right)+\beta I_4(\mu+\nu)\right]\lambda+ \\ + \quad & \beta k\theta(\mu+\nu)I_4^2\left(1-\frac{\theta}{\alpha}I_4\right)+\beta\mu k\frac{\theta^2}{\alpha}I_4^2\left(1-\frac{\theta}{\alpha}I_4\right)=0. \end{aligned}$$

Now, we can try and study the stability of C_4, using Routh-Hurwitz theorem (see theorem (.7) in the Appendix), according to which, for a generic polynomial of third order

$$P(\lambda)=\lambda^3+a_1\lambda^2+a_2\lambda+a_3, \tag{5}$$

the sufficient and necessary conditions in order to have all the roots λ negative or with negative real part are:

$$\begin{cases} a_1>0 \\ a_3>0 \\ a_1a_2-a_3>0. \end{cases}$$

In this case, Routh-Hurwitz conditions correspond to

$$\begin{cases} a_1 = \left[\mu + \beta I_4 + k\theta I_4 \left(1 - \dfrac{\theta}{\alpha} I_4\right)\right] > 0 \\ a_3 = \beta k\theta(\mu+\nu) I_4^2 \left(1 - \dfrac{\theta}{\alpha} I_4\right) + \beta\mu k \dfrac{\theta^2}{\alpha} I_4^2 \left(1 - \dfrac{\theta}{\alpha} I_4\right) > 0 \\ a_1 a_2 - a_3 > 0, \end{cases}$$

with

$$\begin{aligned} a_1 a_2 - a_3 &= (\mu + \beta I_4)\theta^2 I_4^2 \left(1 - \frac{\theta}{\alpha} I_4\right)^2 k^2 + \\ + \quad &\left[\theta(\mu + \beta I_4)^2 I_4 \left(1 - \frac{\theta}{\alpha} I_4\right) - \mu\beta \frac{\theta^2}{\alpha} I_4^2 \left(1 - \frac{\theta}{\alpha} I_4\right)\right] k + \beta I_4(\mu + \beta I_4)(\mu + \nu). \end{aligned}$$

We can immediately notice that the first two conditions are satisfied, and so it remains to establish the sign of $a_1 a_2 - a_3$.
In order to do that, firstly, we can define

$$a := \theta I_4 \left(1 - \frac{\theta}{\alpha} I_4\right), \; b := (\mu + \beta I_4), \; c := \beta I_4(\mu + \nu),$$

so that we can rewrite $a_1 a_2 - a_3$ in the following simpler way:

$$a_1 a_2 - a_3 = b a^2 k^2 + \left[ab^2 - \frac{ac\mu\theta}{\alpha(\mu+\nu)}\right] k + bc. \tag{6}$$

- If $\left[ab^2 - \frac{ac\mu\theta}{\alpha(\mu+\nu)}\right] > 0$, since that $a, b, c, k > 0$, we have

  $$a_1 a_2 - a_3 = b a^2 k^2 + \left[ab^2 - \frac{ac\mu\theta}{\alpha(\mu+\nu)}\right] k + bc > 0.$$

  This implies C_4 is LAS, irrespective of the imitation speed k.

- If $\left[ab^2 - \frac{ac\mu\theta}{\alpha(\mu+\nu)}\right] < 0$, the third Routh-Hurwitz condition might not be satisfied for all values of k.

Let us analyse this latter case in a deeper way:
the second degree equation $a_1 a_2 - a_3 = 0$ has got the following discriminant:

$$\Delta = \left[ab^2 - \frac{ac\mu\theta}{\alpha(\mu+\nu)}\right]^2 - 4a^2 b^2 c.$$

$\longrightarrow$ If $\Delta < 0$ $\left(\Leftrightarrow ab^2 - \frac{ac\mu\theta}{\alpha(\mu+\nu)} > -2ab\sqrt{c}\right)$,

then $sign(a_1a_2 - a_3) = sign(ba^2) > 0$ and so C_4 is still LAS, irrespective of the imitation speed k.
$\longrightarrow$ If $\Delta > 0$ $\left(\Leftrightarrow ab^2 - \frac{ac\mu\theta}{\alpha(\mu+\nu)} < -2ab\sqrt{c}\right)$,
then the second degree equation under consideration admits the following two solutions:

$$k_{1,2} = \frac{-\left[ab^2 - \frac{ac\mu\theta}{\alpha(\mu+\nu)}\right] \mp \sqrt{\Delta}}{2a^2b},$$

with $0 < k_1 < k_2$.
Therefore, if $k \in (0, k_1) \cup (k_2, \infty)$, then $a_1a_2 - a_3 > 0$, and so C_4 is LAS; otherwise, if $k \in (k_1, k_2)$, C_4 is unstable.

Now, we can notice that condition $\Delta < 0$ $\left(\Leftrightarrow ab^2 - \frac{ac\mu\theta}{\alpha(\mu+\nu)} > -2ab\sqrt{c}\right)$ includes the case $\left[ab^2 - \frac{ac\mu\theta}{\alpha(\mu+\nu)}\right] > 0$ and that, through the definitions of a, b and c, we can translate condition $\Delta < 0$ into

$$\mu\theta\beta I_4 < \alpha(\mu + \beta I_4)(\mu + \beta I_4 + 2\sqrt{\beta I_4(\mu + \nu)})$$

and, respectively, $\Delta > 0$ into

$$\mu\theta\beta I_4 > \alpha(\mu + \beta I_4)(\mu + \beta I_4 + 2\sqrt{\beta I_4(\mu + \nu)}).$$

Therefore, the theorem is nearly completely proved.

There remains only to understand the presence of the oscillatority in the sense of Yakubovich.
We are now confined in the case of a value of the imitation speed k that makes C_4 unstable, that is $k \in (k_1, k_2)$.
Under this assumption, the system has four isolated, hyperbolic and unstable equilibria: C_1, C_2, C_3, C_4.
Consequently, hypotheses $H.1$ and $H.3$ of Yakubovich's theorem (see theorem (.8) in the Appendix) are achieved.
Furthermore, since the vector of the state variables $(S(t), I(t), p(t))$ has got $D := \left\{(S, I, p) \in \mathbb{R}^3_+ / S + I \leq 1, p \leq 1\right\}$ as definition set, all solutions of the system are bounded and so also hypothesis $H.2$ is satisfied.
Therefore, thanks to Yakubovich's theorem, the system, in its unstable endemic regime, is oscillatory in the sense of Yakubovich.

The proof is now completed. □

As observed at the end of the Appendix about oscillatority in the sense of

Yakubovich, theorem (.8) does not say anything about the nature of oscillatority. Therefore, it might be interesting to find Hopf bifurcation parameters because they are able to establish the presence of cycles (periodic orbits) for values of those parameters close to bifurcation points.

Corollary 0.2 (Hopf Bifurcation)**.** Let us refer to notations used in the theorem above.
Under appropriate conditions, k is a Hopf bifurcation parameter and k_1, k_2 are Hopf bifurcation critical values.

Proof. We would like to use Poincaré-Andronov-Hopf's theorem with $x_0 = C_4$ and $k_0 = k_{1,2}$ (see theorem (.10) and notations in the Appendix about Hopf bifurcation) .
Because C_4 is an equilibrium for all values of k, in particular $f(C_4, k_{1,2}) = 0$ and so hypothesis 1. of theorem (.10) is immediately satisfied.
The quantity (6) changes its sign according to different values of k. In particular, for $k = k_{1,2}$, it is equal to zero, therefore, for $k = k_{1,2}$ the characteristic polynomial (5) associated to C_4 ceases to have all the eigenvalues with negative real part and it admits a pair of complex conjugate eigenvalues. Consequently, also hypothesis 2. of theorem (.10) is achieved.
Now, let us limit our attention to k_1 (for k_2 analogous considerations hold) and denote with $\pm i\omega$ the pair of complex conjugate eigenvalues that arises at $k = k_1$.
According to the notations used in the proof of theorem above, together with the constant $d := \frac{\beta\mu\theta}{\alpha}$, we can rewrite the characteristic polynomial (5) in function of k as it follows:

$$P(\lambda(k), k) = \lambda(k)^3 + (b + ka)\lambda(k)^2 + (kab + c)\lambda(k) + ka(c + d) = 0. \quad (7)$$

We would like to infer the behavior of $\lambda(k)$ with respect to k; especially, we are looking for its behavior when k is equal to k_1.
Therefore, firstly let us differentiate $P(\lambda(k), k)$ with respect to k and then obtain an expression for $\lambda'(k)$.
Differentiating (7) with respect to k we have

$$3\lambda(k)^2\lambda'(k)+a\lambda(k)^2+2(b+ka)\lambda(k)\lambda'(k)+ab\lambda(k)+(kab+c)\lambda'(k)+a(c+d) = 0,$$

from which we deduce

$$\lambda'(k) = -\frac{a(\lambda(k)^2 + b\lambda(k) + c + d)}{3\lambda(k)^2 + 2(b + ka)\lambda(k) + kab + c}.$$

Putting $k = k_1$ in this last expression, since $\lambda_{1,2}(k_1) = \pm i\omega$, we obtain

$$\lambda'_{1,2}(k_{1,2}) = -\frac{a(-\omega^2 \pm ib\omega + c + d)}{-3\omega^2 \pm 2i(b + k_1 a)\omega + k_1 ab + c}.$$

If we define $A := -\omega^2 + c + d,\ B := 2(b + k_1 a),\ C := -3\omega^2 + k_1 ab + c$ and after removing imaginary parts from the denominator, we have

$$\lambda'_{1,2}(k_{1,2}) = -\frac{a(bB\omega^2 + AC \pm ibC\omega \mp iAB\omega)}{C^2 + B^2\omega^2}.$$

According to the last hypothesis of theorem (5), it must be $Re(\lambda'_{1,2}(k_{1,2})) \neq 0$, which corresponds to $bB\omega^2 + AC \neq 0$.
Therefore, if $bB\omega^2 + AC \neq 0$, that is to say

$$3\omega^4 + \left[2(\mu + \beta I_4)^2 + k_1\theta I_4(\mu + \beta I_4)\left(1 - \frac{\theta}{\alpha}I_4\right)(2 - \beta I_4(\mu + \nu))\right]\omega^2 -$$

$$-\left[3\left(\beta I_4(\mu + \nu) + \frac{\beta\mu\theta}{\alpha}\right)\right]\omega^2 +$$

$$+\left(\beta I_4(\mu + \nu) + \frac{\beta\mu\theta}{\alpha}\right)\left(k_1\theta I_4(\mu + \beta I_4)\left(1 - \frac{\theta}{\alpha}I_4\right) + \beta I_4(\mu + \nu)\right) \neq 0,$$

(this is the appropriate condition the corollary refers to), all the hypotheses of theorem (5) are satisfied and so k is a Hopf bifurcation parameter and k_1 (and k_2) is a Hopf bifurcation critical value.

□

0.10.5 Equilibria and their stability: summary

To better understand the full picture of equilibrium points and their stability, here it is a summary:

- a pre-vaccination $DFE,\ C_1 = (1, 0, 0)$, that is always (irrespective of the imitation speed k) unstable,
- a pure-vaccinator $DFE,\ C_2 = (0, 0, 1)$, that is always unstable,
- a pre-vaccination $EE,\ C_3 = \left(R_0^{-1}, \frac{\mu p_c}{\mu+\nu}, 0\right)$, that is always unstable,
- an EE with positive vaccine uptake, $C_4 = \left(R_0^{-1}, \frac{p_c}{1+\frac{\nu}{\mu}+\frac{\theta}{\alpha}}, \frac{\theta}{\alpha}\frac{p_c}{1+\frac{\nu}{\mu}+\frac{\theta}{\alpha}}\right)$, that is unstable for an intermediate window of values of the imitation coefficient k, while both slow and fast imitation are stabilizing forces. Furthermore, it is LAS, irrespective to k, also for some combinations of the values of parameters $R_0, \mu, \nu, \alpha, \theta, \beta$.

From the analysis of this summary, since that DFE points, C_1 and C_2, are always unstable, while the EE point C_4 can become LAS for some values of the imitation speed k, we can infer the IMPOSSIBILITY of disease ERADICATION associated to $I - model$.
Furthermore, $I - model$ allows pre-vaccination equilibria (C_1 and C_3), even if they are always unstable.
In the following chapter it will be considered another model that, together with other merits, will improve this imitation-related negative aspects.

0.11 Simulations

To better understand the impact of $VSEs$ on the dynamics of immunization programs I made some specific simulations using MATLAB and I considered the following values of demo-epidemiological parameters:

- the life expectancy $L = \frac{1}{\mu}$ is set to 78 $years$, which is representative of mortality in modern industrialized countries (in particular of Italian mortality at the beginning of 2000);
- the Basic Reproduction Number R_0 is set to 15, which corresponds to that of measles;
- the recovery rate ν is set to $\frac{1}{7}\ days^{-1} = \frac{365}{7}\ years^{-1}$, which corresponds to that of measles.

With these values, equilibria become: $C_1 = (1, 0, 0),\ C_2 = (0, 0, 1)$,

$$C_3 = \left(\frac{1}{15}, 2.294 \times 10^{-4}, 0\right),\ C_4 = \left(\frac{1}{15}, \frac{\frac{14}{15}}{1 + \frac{28470}{7} + \frac{\theta}{\alpha}}, \frac{\theta}{\alpha}\frac{\frac{14}{15}}{1 + \frac{28470}{7} + \frac{\theta}{\alpha}}\right).$$

As we can see, the value of C_4 depends on the quantity $\frac{\theta}{\alpha}$, which now we rename with $\bar{\alpha} = \frac{\alpha}{\theta}$.
I computed three different values of $\bar{\alpha}$, according to three different values of vaccine uptake against measles observed in Italy in three different years between 1996 and 2008 :

$$p^{1996} = 0.56,\ p^{2003} = 0.78,\ p^{2008} = 0.90$$

(these data are reported in the introduction).
Putting the specific Italian vaccine fractions equal to that of C_4, that is to say

$$p^i = \frac{p_c}{\bar{\alpha}\left(1 + \frac{\nu}{\mu} + \frac{1}{\bar{\alpha}}\right)},\ for\ i = 1996, 2003, 2008,$$

we can infer

$$\bar{\alpha} = \frac{p_c - p^i}{\left(1 + \frac{\nu}{\mu}\right) p^i}, \ for \ i = 1996, 2003, 2008.$$

Consequently, I found, respectively,

$$\bar{\alpha}^{1996} = 1.638 \times 10^{-4}, \ \bar{\alpha}^{2003} = 0.483 \times 10^{-4}, \ \bar{\alpha}^{2008} = 0.091 \times 10^{-4}.$$

I studied the impact of $VSEs$ on the transient infection dynamics triggered by a new vaccination endemic state. The vaccine is introduced at time $t = 0$, with initial vaccine uptake set to 0.95 . $VSEs$ occur from the beginning of the program.

Initial condition. For my simulations I used the following initial condition

$$(S_0, I_0, p_0) = \left(\frac{1}{15}, 2.294 \times 10^{-4}, 0.95\right).$$

Choice of the value of the product $k\theta$.
Note that a single value of $\bar{\alpha}$ is compatible with a wide variety of dynamic endemic regimes, depending on the product $k\theta$, as is clear by reparametrizing the equation of $p(t)$ in system (4), as it follows:

$$p' = k\theta p(1-p)(I - \bar{\alpha}p).$$

I choosed a value of the product $k\theta$ that could allow an oscillatory endemic regime in all cases (for the three different values of $\bar{\alpha}$ found).
In order to do that, firstly, I read the third Routh-Hurwitz condition for point C_4, see expression (6), as a second degree equation with respect to ak instead of k alone, that is

$$b(ak)^2 + \left[b^2 - \frac{c\mu\theta}{\alpha(\mu+\nu)}\right](ak) + bc = 0.$$

This latter equation admits the following solutions:

$$(ak)_{1,2} = \frac{-\left[b^2 - \frac{c\mu\theta}{\alpha(\mu+\nu)}\right] \mp \sqrt{\frac{\Delta}{a^2}}}{2b},$$

where $\Delta = \left(ab^2 - \frac{ac\mu\theta}{\alpha(\mu+\nu)}\right)^2 - 4a^2b^2c$.

Remembering the definition of a, that is $a := \theta I_4 \left(1 - \frac{I_4}{\bar{\alpha}}\right)$, we can infer the following expression for the product $k\theta$:

$$k\theta = \frac{ak}{\left(1 - \frac{I_4}{\bar{\alpha}}\right) I_4}.$$

Therefore, we can traslate the solutions above in terms of $k\theta$ as it follows:

$$(k\theta)_{2,1} = \frac{(ak)_{1,2}}{\left(1 - \frac{I_4}{\bar{\alpha}}\right) I_4}.$$

Considering now the different values of $\bar{\alpha}$ found, we can compute the oscillatory window for $k\theta$ in each case:

- if $\bar{\alpha} = \bar{\alpha}^{1996}$, then $I_4 = \bar{\alpha}^{1996} p^{1996}$ and so, remembering the definitions of a, b and c, we have all the ingradients to compute firstly $(ak)_{1,2}$ and then $(k\theta)_{2,1}$.

  Therefore, in this first case, I found that, in order to be in the oscillatory endemic regime, $k\theta$ should range between $(k\theta)_1 = 1399.5$ and $(k\theta)_2 = 1.642 \times 10^6$;

- if $\bar{\alpha} = \bar{\alpha}^{2003}$, then $I_4 = \bar{\alpha}^{2003} p^{2003}$ and so, in this second case, an oscillatory endemic regime is achieved through values of $k\theta$ ranging between $(k\theta)_1 = 1002.9$ and $(k\theta)_2 = 2.231 \times 10^7$;

- if $\bar{\alpha} = \bar{\alpha}^{2008}$, then $I_4 = \bar{\alpha}^{2008} p^{2008}$ and so, in this third case, an oscillatory endemic regime is achieved through values of $k\theta$ ranging between $(k\theta)_1 = 869.166$ and $(k\theta)_2 = 5.732 \times 10^8$.

Consequently, in order to have an oscillatory endemic regime in all cases, the product $k\theta$ should be taken into the following window of values:

$$k\theta \in (1399.5,\ 1.642 \times 10^6).$$

In particular, I choosed a value of $k\theta = 5000$ for my simulations.

To better understand the role played by the imitation speed k and by the perceived probability α of suffering a VSE as consequence of vaccination, let us focus on the product $k\alpha$, that can be obtained from

$$k\alpha = k\theta \frac{\alpha}{\theta} = k\theta\bar{\alpha}.$$

In particular, we have three values of $k\alpha$ according to the three values of $\bar{\alpha}$ found, that is to say

$$k\alpha = k\theta\bar{\alpha}^{1996},\ k\theta\bar{\alpha}^{2003},\ k\theta\bar{\alpha}^{2008} = 0.819,\ 0.241,\ 0.045.$$

Let us firstly concentrate on the dynamics of $Re(t), I(t)$ and $p(t)$ (note that the Effective Reproduction Number $Re(t)$ is used instead of the state variable $S(t)$) for just one value of the product $k\alpha$, for example for $k\alpha = 0.819$ and for a time horizon of 140 years.
As we can see from figure (2) , the system seems to converge to a stable limit cycle.
The vaccine uptake starts declining soon after the program starts, due to the onset of $VSEs$. Thus, the Effective Reproduction Number $Re(t)$ initially declines, but then increases and exceeds the unit threshold at $t \approx 5$ years, yielding a new epidemic outbreak at $t \approx 8$ years.

Looking now at the dynamics of $p(t)$ and $I(t)$ for the three different values of $k\alpha$ found and for a time horizon of 140 years (see figure (3)), we can notice that (i) the average uptake decreases in k, (ii) the amplitude of oscillations of $p(t)$ increases in k, (iii) the duration of the period between the start of the program and a new epidemic outbreak decreases in k.
We can give an explanation of points (i) and (ii) if we notice that slow values of product $k\alpha$ correspond to slow values of α, for fixed k. Therefore, slow values of $k\alpha$ are linked to small probabilities of suffering $VSEs$ and so they allow high average uptakes and small amplitude of vaccine oscillations.
We can give an explanation of point (iii) if we notice that slow values of product $k\alpha$ correspond to slow values of k, for fixed α. Therefore, slow values of $k\alpha$ are linked to low spread of information that slows down the reactivity of the vaccine uptake to changes in the pay-off gain and so large time passes from the start of the programme and a new epidemic outbreak.

For example, the "low" $k\alpha$ value ($k\alpha = 0.045$) yields oscillations in vaccine uptake that are of small amplitude and they are confined around high values of $p(t)$ (between 0.8 and 1). Moreover, there is an interval of 45 years about before a new epidemic, which is only a few years long for $k\alpha = 0.819$.
Furthermore, note that for small $k\alpha$ the infection prevalence is close to zero.

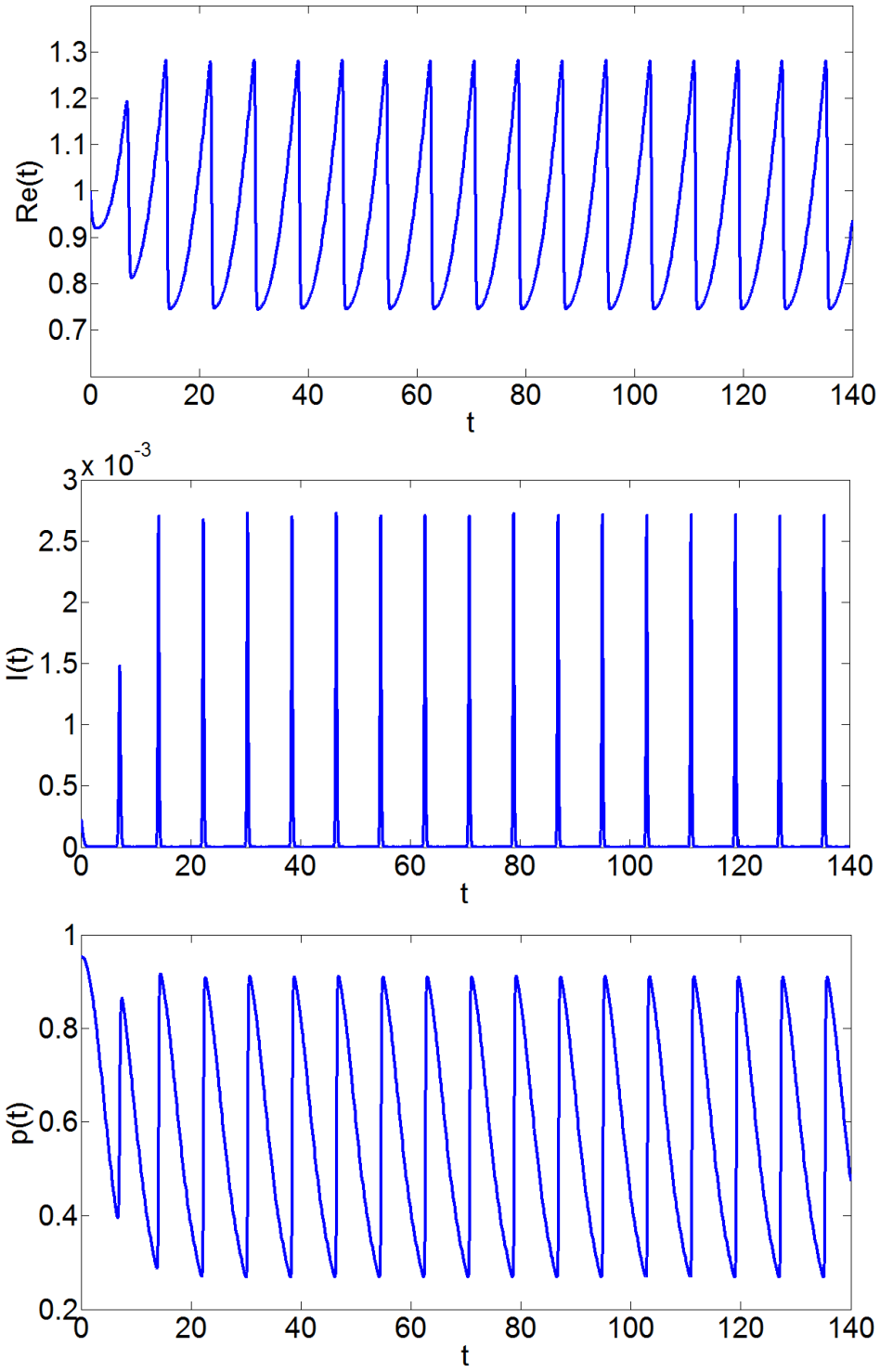

Figure 2: $I-model$ and the dynamics of $Re(t)$ (top row), $I(t)$ (central row) and $p(t)$ (bottom row) with a value of $k\alpha$ set to 0.819 .

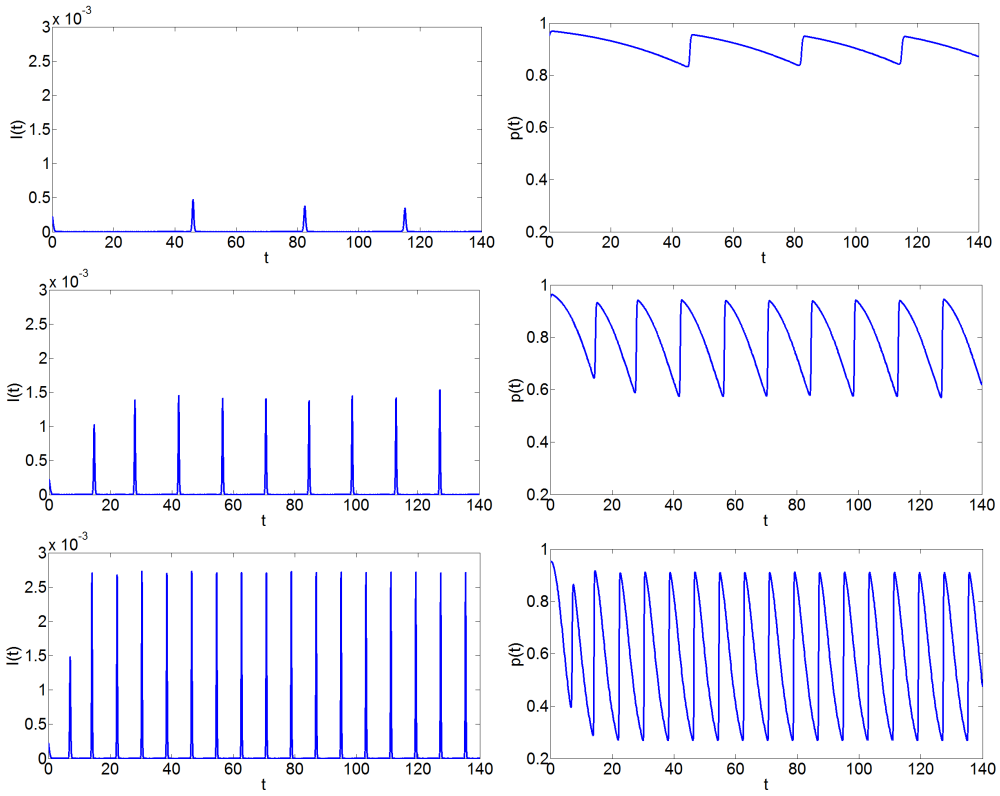

Figure 3: $I - model$ and the dynamics of $I(t)$ (left column) and $p(t)$ (right column) for three different values of $k\alpha$: $k\alpha = 0.045$ (top row), $k\alpha = 0.241$ (central row), $k\alpha = 0.819$ (bottom row).

The interplay of public intervention and private choices in determining the outcome of vaccination programs

0.12 The model: G-model

Unlike the previous $I - model$, where the behavior perceived as optimal is assumed to spread in the population through imitation alone, that is to say via information exchanged essentially during social contacts through person-to-person interactions, now we assume that behavior can also spread through information provided by the Public Health system (PHS).
Therefore, we expand the dynamic equation for the vaccine uptake $p(t)$ in (4), to include public information, as it follows:

$$p' = k\Delta E p(1-p) + k_G \Delta E_G (1-p). \tag{8}$$

The first part of (8) models the change in vaccine uptake arising from information exchanged during social contacts between parents who vaccinate and parents not vaccinating and it is exactly the equation describing the dynamics of vaccination in $I - model$.
The second part of (8) models the change in vaccine uptake arising from the PHS to families who did not vaccinate (note that the public contribution does not include the p term).
In the previous section, we have already seen the meaning of the quantities present in the private contribution.
In the same way, we can describe ΔE_G as the pay-off gain of vaccination perceived from information spread by the PHS through its channels and k_G as the "public acceptance" coefficient, tuning the speed at which new vaccinators are created by public information.

We can develop ΔE_G analogously to ΔE, but, actually, we hypothesize for it a much simpler form.
Indeed, messages from the PHS aim to communicate that vaccines, besides being effective, are highly safe, with a very low, constant, risk of VSE, and that the risk of disease is prevalence-indipendent. The latter is obviously motivated by the need to avoid coverage decline during periods of falling prevalence (for example after a period of persistently high vaccine uptake). Therefore, we assume that ΔE_G is simply constant.
By defining

$$\frac{k_G}{k}\Delta E_G := \gamma \geq 0$$

and together with the already considered assumptions on ΔE, we end up with the following equation for the vaccinated proportion:

$$p' = k(1-p)\left[(\theta I - \alpha p)p + \gamma\right].$$

The parameter γ is the perceived pay-off gain from adopting the public recommendation weighted by the ratio $\frac{k_G}{k}$ between the relative speeds of public and private information, which tunes the effectiveness of the public actions (information, education, availability of vaccination infrastructures, including monetary subsidies to vaccination staff) in affecting perceptions on vaccines and disease.
The resulting model (let us name it $G-model$), which includes both private and public interventions, is:

$$\begin{cases} S' = \mu(1-p) - \mu S - \beta SI \\ I' = \beta SI - (\mu+\nu)I \\ p' = k(1-p)\left[(\theta I - \alpha p)p + \gamma\right] \end{cases} \tag{9}$$

Note that, if $\gamma = 0$, we obtain the already known $I-model$ (4).
Therefore, since now on, we consider $\gamma > 0$ in reference to $G-model$ (9).

0.13 Equilibria

We can find equilibrium points of system (9) from setting the derivatives of the state variables equal to zero:

$$\begin{cases} S' = \mu(1-p) - \mu S - \beta SI = 0 \\ I' = \beta SI - (\mu+\nu)I = 0 \\ p' = k(1-p)\left[(\theta I - \alpha p)p + \gamma\right] = 0. \end{cases}$$

Let us start looking at the values of S, I, p that satisfy the second equation $I' = \beta SI - (\mu+\nu)I = 0$, that is to say $I = 0$ or $S = R_0^{-1}$.

- If $I = 0$, then the equations reduce to

$$\begin{cases} S' = \mu(1-p) - \mu S = 0 \\ I = 0 \\ p' = k(1-p)(-\alpha p^2 + \gamma) = 0. \end{cases}$$

Therefore, from the first equation we infer that $S = 1 - p$ and from the third one that $p = 1$ or p satisfies $-\alpha p^2 + \gamma = 0$.
If $p = 1 \Longrightarrow S = 0 \Longrightarrow$ we find the pure-vaccinator DFE point $E_1 = (0, 0, 1)$.
If p satisfies $-\alpha p^2 + \gamma = 0$, since $0 \leq p < 1$, we obtain another equilibrium point if and only if $\gamma < \alpha := \gamma_1$.
Therefore, under condition $\gamma < \gamma_1$, $p = \sqrt{\frac{\gamma}{\alpha}} := p_2 \Longrightarrow S = 1 - p_2 \Longrightarrow$ we find the DFE point with positive vaccine uptake $E_2 = (1 - p_2, 0, p_2)$.

- If $I \neq 0$, then $S = R_0^{-1}$ and the equations become:

$$\begin{cases} S' = \mu(1-p) - \mu R_0^{-1} - (\mu + \nu)I = 0 \\ S = R_0^{-1} \\ p' = k(1-p)\left[(\theta I - \alpha p)p + \gamma\right] = 0. \end{cases}$$

From the third equation we infer that $p = 1$ or p satisfies $(\theta I - \alpha p)p + \gamma = 0$.
If $p = 1 \Longrightarrow I = -\frac{\mu}{\beta} < 0 \Longrightarrow$ no new equilibria are generated.
If p satisfies $(\theta I - \alpha p)p + \gamma = 0$, under specific conditions that will be specified later on, we can find the EE point $E_3 = (R_0^{-1}, I_3, p_3)$, with (I_3, p_3) the unique solution of the following system:

$$\begin{cases} \dfrac{\mu}{\mu + \nu}(1-p) - \dfrac{\mu}{\beta} - I = 0 \\ (\theta I - \alpha p)p + \gamma = 0. \end{cases} \tag{10}$$

Now, let us compute the Jacobian matrix associated to system (9) in order to analyse the local stability of equilibria:

$$J = \begin{pmatrix} \frac{\partial S'}{\partial S} & \frac{\partial S'}{\partial I} & \frac{\partial S'}{\partial p} \\ \frac{\partial I'}{\partial S} & \frac{\partial I'}{\partial I} & \frac{\partial I'}{\partial p} \\ \frac{\partial p'}{\partial S} & \frac{\partial p'}{\partial I} & \frac{\partial p'}{\partial p} \end{pmatrix} = \begin{pmatrix} -\mu - \beta I & -\beta S & -\mu \\ \beta I & \beta S - (\mu + \nu) & 0 \\ 0 & k\theta(1-p)p & \frac{\partial p'}{\partial p} \end{pmatrix}$$

where

$$\frac{\partial p'}{\partial p} = -k\left[(\theta I - \alpha p)p + \gamma\right] + k(1-p)\left[-2\alpha p + \theta I\right].$$

0.13.1 Stability of the pure-vaccinator DFE E_1

The Jacobian matrix at $E_1 = (0, 0, 1)$ is

$$J_{|E_1} = \begin{pmatrix} -\mu & 0 & -\mu \\ 0 & -(\mu+\nu) & 0 \\ 0 & 0 & -k(-\alpha+\gamma) \end{pmatrix}.$$

The linearized equation for p at the equilibrium reads

$$\eta' = -k(-\alpha+\gamma)\eta.$$

Therefore, if $\underline{\gamma < \gamma_1 = \alpha}$, then $-k(-\alpha+\gamma) > 0$, and so $\underline{E_1}$ is $\underline{unstable}$.

If $\underline{\gamma > \gamma_1}$, we can show that $\underline{E_1}$ is $\underline{GAS}$:

Proof. Since that $I \geq 0$ and $p \leq 1$, we have

$$p' = k(1-p)((\theta I - \alpha p)p + \gamma) \geq k(1-p)(-\alpha p + \gamma).$$

Let us find the general solution $p_*(t)$ of $p' := k(1-p)(-\gamma_1 p + \gamma)$.
Therefore, we should assume $p \neq 1,\ p \neq \frac{\gamma}{\gamma_1}$ and integrate both sides of

$$\frac{dp}{(1-p)(-\gamma_1 p + \gamma)} = kdt.$$

From the equality

$$\frac{A}{1-p} + \frac{B}{\gamma - \gamma_1 p} = \frac{1}{(1-p)(\gamma - \gamma_1 p)},$$

we infer that $A = \frac{1}{\gamma - \gamma_1}$ and $B = \frac{-\gamma_1}{\gamma - \gamma_1}$.
Consequently, for a certain constant C_1, we can write

$$\begin{aligned} kt + C_1 &= \int \frac{dp}{(1-p)(-\gamma_1 p + \gamma)} = \frac{1}{\gamma - \gamma_1}\left[\int \frac{dp}{(1-p)} - \int \frac{\gamma_1 dp}{\gamma - \gamma_1 p}\right] = \\ &= \frac{1}{\gamma - \gamma_1}\left[-ln(1-p) + ln(\gamma - \gamma_1 p)\right] = \frac{1}{\gamma - \gamma_1} ln\left(\frac{\gamma - \gamma_1 p}{1-p}\right) \end{aligned}$$

from which we obtain

$$\frac{\gamma - \gamma_1 p}{1-p} = C \exp\left(k(\gamma - \gamma_1)t\right),$$

where $C := \exp\left(C_1(\gamma - \gamma_1)\right) > 0$.

Finally, extracting p, we infer the following general solution:

$$p_*(t) = \frac{\gamma - C\exp\left(k(\gamma-\gamma_1)t\right)}{\gamma_1 - C\exp\left(k(\gamma-\gamma_1)t\right)}.$$

Therefore, since $k(\gamma-\gamma_1) > 0,\ \lim_{t\to\infty} p_*(t) = 1$.
Consequently, using comparison properties for differential equations, we can write

$$1 = \lim_{t\to\infty} p_*(t) \leq \liminf_{t\to\infty} p(t) \leq \limsup_{t\to\infty} p(t) \leq 1.$$

This implies

$$\lim_{t\to\infty} p(t) = 1.$$

Reading now the equation $S' = \mu(1-p) - \mu S - \beta SI$ for long time, it "becomes" $S' = -\mu S - \beta SI$.
But, since $I \geq 0,\ S' = -\mu S - \beta SI \leq -\mu S$.
The differential equation defined by $S' := -\mu S$ admits a general solution $S_*(t)$ of the form

$$S_*(t) = C_2\exp\left(-\mu t\right),$$

with C_2 a positive constant.
Therefore, using comparison properties for differential equations, we can write

$$0 \leq \liminf_{t\to\infty} S(t) \leq \limsup_{t\to\infty} S(t) \leq \lim_{t\to\infty} S_*(t) = 0.$$

And so,

$$\lim_{t\to\infty} S(t) = 0.$$

Reading now also the equation $I' = \beta SI - (\mu+\nu)I$ for long time, it "becomes" $I' = -(\mu+\nu)I$, which admits the following general solution

$$I(t) = C_3\exp\left(-(\mu+\nu)t\right),$$

with C_3 a positive constant.
This implies

$$\lim_{t\to\infty} I(t) = 0.$$

In conclusion, summarizing, we have shown that

$$\lim_{t\to\infty}(S(t), I(t), p(t)) = (0,0,1) = E_1,$$

which means E_1 is GAS.

□

0.13.2 Stability of the $DFE\ E_2$

For the existence condition on E_2, now we assume to be in the case $\underline{\gamma < \gamma_1}$.
The Jacobian matrix at $E_2 = (1 - p_2, 0, p_2)$ is

$$J_{|E_2} = \begin{pmatrix} -\mu & -\beta(1-p_2) & -\mu \\ 0 & \beta(1-p_2) - (\mu+\nu) & 0 \\ 0 & k\theta(1-p_2)p_2 & -2\alpha k(1-p_2)p_2 \end{pmatrix}.$$

The linearized equation for I at the equilibrium reads

$$i' = [\beta(1-p_2) - (\mu+\nu)]\, i = \beta\left[1 - p_2 - R_0^{-1}\right] i = \beta(p_c - p_2)i.$$

Therefore, if $\underline{p_c > p_2}(\leftrightarrow p_c > \sqrt{\frac{\gamma}{\alpha}} \leftrightarrow \underline{\gamma < \alpha p_c^2 := \gamma_c})$, then $\underline{E_2}$ is $\underline{unstable}$.

If $\underline{\gamma > \gamma_c}$, we can show that $\underline{E_2}$ is $\underline{GAS}$:

Proof. Since that $I \geq 0$ and $p_2 := \sqrt{\frac{\gamma}{\alpha}}$ we have

$$p' = k(1-p)((\theta I - \alpha p)p + \gamma) \geq k(1-p)(-\alpha p^2 + \alpha p_2^2) = \alpha k(1-p)(p_2+p)(p_2-p),$$

and using also $p \geq 0$, we can infer that

$$p' \geq \alpha k p_2 (1-p)(p_2 - p).$$

Let us find the general solution $p_*(t)$ of $p' := \alpha k p_2 (1-p)(p_2-p)$.
Therefore, we should assume $p \neq 1,\ p \neq p_2$ and integrate both sides of

$$\frac{dp}{(1-p)(p_2-p)} = \alpha k p_2 dt.$$

From the equality

$$\frac{A}{1-p} + \frac{B}{p_2 - p} = \frac{1}{(1-p)(p_2-p)},$$

we infer that $A = \frac{1}{p_2 - 1}$ and $B = -\frac{1}{p_2 - 1}$.
Consequently, for a certain constant C_1, we can write

$$\begin{aligned} \alpha k p_2 t + C_1 &= \int \frac{dp}{(1-p)(p_2-p)} = \frac{1}{p_2-1}\left[\int \frac{dp}{(1-p)} - \int \frac{dp}{p_2 - p}\right] = \\ &= \frac{1}{p_2 - 1}\left[-ln(1-p) + ln|p_2 - p|\right] = \frac{1}{p_2-1} ln\left(\frac{|p_2 - p|}{1-p}\right) \end{aligned}$$

Putting $C := \exp(C_1(p_2 - 1))$ and using $p \geq 0$, we obtain that $p_*(t)$ satisfies

$$|p_2 - p_*| = (1-p)C\exp(\alpha k p_2(p_2-1)t) \leq C\exp(\alpha k p_2(p_2-1)t)$$

Therefore, since $\alpha k p_2(p_2 - 1) < 0$,

$$\lim_{t\to\infty} |p_2 - p_*| \leq \lim_{t\to\infty} C\exp(\alpha k p_2(p_2-1)t) = 0,$$

that implies

$$\lim_{t\to\infty} p_*(t) = p_2.$$

Consequently, using comparison properties for differential equations, we have

$$p_2 = \lim_{t\to\infty} p_*(t) \leq \liminf_{t\to\infty} p(t) \leq \lim_{t\to\infty} p(t).$$

Reading now the equation $S' = \mu(1-p) - \mu S - \beta SI$ for long time, since $\lim_{t\to\infty} p(t) \geq p_2$ and $I, S \geq 0$, we have

$$S' \leq \mu(1-p_2) - \mu S = \mu(1 - p_2 - S).$$

Let us find the general solution $S_*(t)$ of $S' := \mu(1 - p_2 - S)$.
Integrating $\frac{dS}{(1-p_2-S)} = \mu dt$, we obtain that $S_*(t)$ satisfies

$$|1 - p_2 - S_*| = C_2\exp(-\mu t),$$

with C_2 a positive constant.
Therefore,

$$\lim_{t\to\infty} S_*(t) = 1 - p_2.$$

And so, for comparison,

$$\lim_{t\to\infty} S(t) \leq \limsup_{t\to\infty} S(t) \leq \lim_{t\to\infty} S_*(t) = 1 - p_2.$$

Reading now also the equation $I' = \beta I(S - R_0^{-1})$ for long time, since $\lim_{t\to\infty} S(t) \leq 1 - p_2$, we have

$$I' \leq \beta I(1 - p_2 - R_0^{-1}) = \beta I(p_c - p_2).$$

But the differential equation defined by $I' := \beta I(p_c - p_2)$ admits a general solution $I_*(t)$ of the form

$$I_*(t) = C_3\exp(\beta(p_c - p_2)t),$$

with C_3 a positive constant.

Therefore, since we are in the case $\gamma > \gamma_c$, that is to say $p_2 > p_c$, we have

$$\lim_{t\to\infty} I_*(t) = 0,$$

and so, for comparison,

$$0 \leq \liminf_{t\to\infty} I(t) \leq \limsup_{t\to\infty} I(t) \leq \lim_{t\to\infty} I_*(t) = 0.$$

This implies

$$\lim_{t\to\infty} I(t) = 0$$

Let us return now to the equation for p'.
Since $\lim_{t\to\infty} I(t) = 0$ and $p \leq 1$, for long time, we have

$$p' = \alpha k(1-p)(p_2+p)(p_2-p) \leq \alpha k(1-p)(p_2+1)(p_2-p).$$

Through an already seen integration, we can see that the general solution $\tilde{p}(t)$ of $p' = \alpha k(1-p)(p_2+1)(p_2-p)$ satisfies

$$|p_2 - \tilde{p}| = (1-p)C_4 \exp\left(\alpha k(p_2+1)(p_2-1)t\right) \leq C_4 \exp\left(\alpha k(p_2+1)(p_2-1)t\right),$$

with C_4 a positive constant.
Therefore, for comparison,

$$\limsup_{t\to\infty} p(t) \leq \lim_{t\to\infty} \tilde{p}(t) = p_2,$$

and so, together with what we have already seen, we can write the following chain of inequalities:

$$p_2 \leq \liminf_{t\to\infty} p(t) \leq \limsup_{t\to\infty} p(t) \leq p_2.$$

This implies

$$\lim_{t\to\infty} p(t) = p_2.$$

Let us come back now also to the equation for S'.
Since $\lim_{t\to\infty} I(t) = 0$ and $\lim_{t\to\infty} p(t) = p_2$, for long time, it "becomes" $S' = \mu(1-p_2-S)$.
But we have already seen that the latter equation admits a general solution $S(t)$ satisfying

$$|1 - p_2 - S| = C_5 \exp(-\mu t),$$

with C_5 a positive constant.
Therefore,

$$\lim_{t\to\infty} S(t) = 1 - p_2.$$

Summarizing, we have shown that

$$\lim_{t\to\infty} (S(t), I(t), p(t)) = (1-p_2, 0, p_2) = E_2,$$

which means E_2 is GAS. □

0.13.3 Existence and uniqueness of the EE E_3

We have seen, in the section about $G-model$ equilibria, that another equilibrium point $E_3 = (R_0^{-1}, I_3, p_3)$ may come from finding a (the) solution (I_3, p_3) of system (10), that is to say of the following system:

$$\begin{cases} I = \dfrac{\mu}{\mu+\nu}(p_c - p) \\ I = -\dfrac{\gamma}{\theta p} + \dfrac{\alpha p}{\theta}. \end{cases}$$

We can translate this purpose into a problem of finding conditions of existence and uniqueness on the possible intersections between the curves, in the plane (p, I) restricted to $0 \leq I, p \leq 1$, defined by functions

$$f(p) := \frac{\mu}{\mu+\nu}(p_c - p) \; and \; g(p) := -\frac{\gamma}{\theta p} + \frac{\alpha p}{\theta}.$$

As we can see, $f(p)$ is a straight line with negative slope that intersects the $I - axis$ in $I_f = \frac{\mu p_c}{\mu+\nu}$ and the $p - axis$ in $p_f = p_c$, while $g(p)$ is an increasing function $\left(g'(p) = \frac{\gamma}{\theta p^2} + \frac{\alpha}{\theta} > 0\right)$ that intersects the $p-axis$ in $p_g = \sqrt{\frac{\gamma}{\alpha}} = p_2$.
In order to better imagine the situation, look at figure (4).
Note that I obtained that figure, through MATLAB, using the following completely deceptive values of paremeters:

$$\frac{\gamma}{\theta} = 0.08, \frac{\alpha}{\theta} = 0.5, \frac{\mu}{\mu+\nu} = 0.9, p_c = 0.89.$$

We want now to study conditions on possible intersections between f and g. Firstly, let us compute the values of the two functions at the right extreme point of their domain:

$$f(1) = -\frac{\mu R_0^{-1}}{\mu+\nu} < 0, \; g(1) = -\frac{\gamma}{\theta} + \frac{\alpha}{\theta}.$$

Therefore, the two graphics can intersect in a positive value of I only if $g(1) > 0$, that is to say only if $\gamma < \alpha = \gamma_1$.
Furthermore, looking at the intersection points, p_f and p_g, with $p - axis$, we infer that in order to have one (and only one) intersection, between f and g, it must happen also that $p_2 < p_c (\leftrightarrow \gamma < \gamma_c)$.
In conclusion, putting the above observations together and noticing that $\gamma_c < \gamma_1$, we have proved that functions f and g intersect in one and only one point (I_3, p_3), with $0 < I_3 < 1$ and $0 < p_3 < 1$, if and only if $\gamma < \gamma_c$.

Consequently, we have shown that if $\gamma < \gamma_c$, one and only one EE point $E_3 = (R_0^{-1}, I_3, p_3)$ appears, where the couple (I_3, p_3) satisfies system (10), with $0 < I_3 < \frac{\mu p_c}{\mu+\nu}$ and $p_2 < p_3 < 1$ (as we can see from figure (4)).

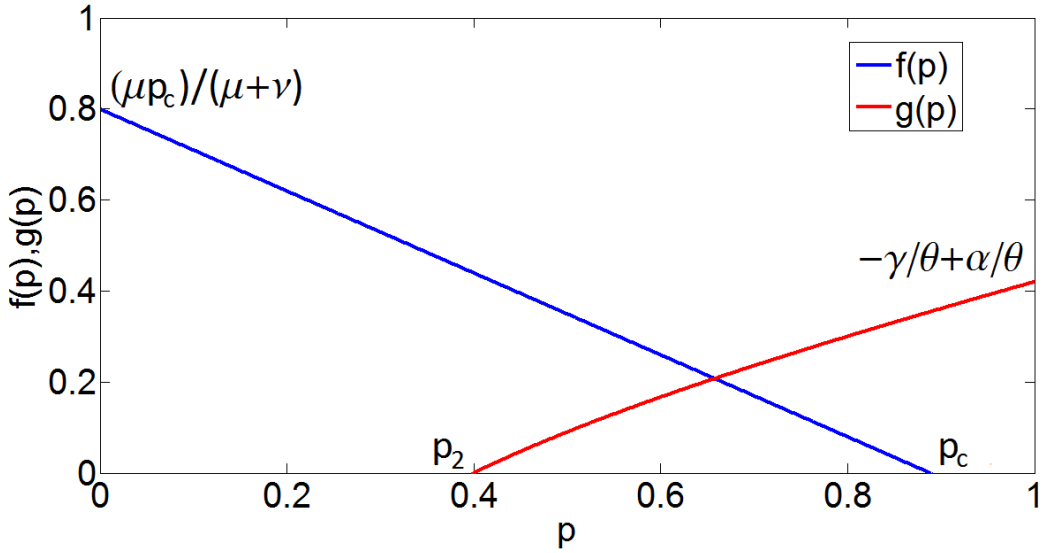

Figure 4: Graphics of functions f and g in the plane (p, I) restricted to $0 \leq I, p \leq 1$.

0.13.4 Stability of the EE E_3

For the existence condition on E_3, we now assume to be in the case $\gamma < \gamma_c$. The study of the stability of E_3 can be summarized by the following theorem:

Theorem 0.3 (Stability of the EE E_3)**.**
(A) If $\gamma > \hat{\gamma}$, where

$$\hat{\gamma} = p_3^2 \left[\frac{\mu\theta\beta I_3}{(\mu + \beta I_3)(\mu + \beta I_3 + 2\sqrt{\beta I_3(\mu + \nu)})} - \alpha \right]$$

then E_3 is LAS.
(B) If $\gamma < \hat{\gamma}$ two values $u_1,\ u_2$, with $0 < u_1 < u_2$, exist such that

1. if $\psi := k\theta I_3(1 - p_3)p_3 \in (0, u_1) \cup (u_2, \infty)$, then E_3 is LAS,

2. if $\psi \in (u_1, u_2)$, then E_3 is *unstable* and the system is oscillatory in the sense of Yakubovich.

Proof. Firstly, let us write down the Jacobian matrix at $E_3 = (R_0^{-1}, I_3, p_3)$:

$$J_{|E_3} = \begin{pmatrix} -(\mu + \beta I_3) & -(\mu + \nu) & -\mu \\ \beta I_3 & 0 & 0 \\ 0 & \frac{\partial p'}{\partial I}_{|E_3} & \frac{\partial p'}{\partial p}_{|E_3} \end{pmatrix},$$

where,

$$\frac{\partial p'}{\partial I}_{|E_3} = k\theta(1-p_3)p_3$$

and, using the equation satisfied by I_3 and p_3, coming from system (10), that is to say $\theta I_3 = -\frac{\gamma}{p_3} + \alpha p_3$, we have

$$\begin{aligned}\frac{\partial p'}{\partial p}_{|E_3} &= k(1-p_3)(-2\alpha p_3 + \theta I_3) = k(1-p_3)\left(-2\alpha p_3 - \frac{\gamma}{p_3} + \alpha p_3\right) = \\ &= -k(1-p_3)\left(\alpha p_3 + \frac{\gamma}{p_3}\right) = -k\theta(1-p_3)p_3\frac{1}{\theta}\left(\alpha + \frac{\gamma}{p_3^2}\right).\end{aligned}$$

Therefore, if we define $\psi := k\theta(1-p_3)p_3$ and $A := \frac{1}{\theta}\left(\alpha + \frac{\gamma}{p_3^2}\right)$, the Jacobian matrix reduces to

$$J_{|E_3} = \begin{pmatrix} -(\mu+\beta I_3) & -(\mu+\nu) & -\mu \\ \beta I_3 & 0 & 0 \\ 0 & \psi & -A\psi \end{pmatrix}.$$

The corresponding characteristic polynomial is:

$$\begin{aligned} - \quad & det(J_{|E_3} - \lambda Id) = \lambda^3 + (\mu + \beta I_3 + A\psi)\lambda^2 + \\ + \quad & [(\mu+\beta I_3)A\psi + \beta I_3(\mu+\nu)]\,\lambda + \beta I_3\,[(\mu+\nu)A\psi + \mu\psi] = 0. \end{aligned}$$

We can rewrite this latter equation in the following more understandable way:

$$\lambda^3 + a_1\lambda^2 + a_2\lambda + a_3 = 0$$

where

$$\begin{cases} a_1 = A\psi + q_2, \qquad q_2 = \mu + \beta I_3; \\ a_2 = A\psi q_2 + q_1, \qquad q_1 = \beta I_3(\mu+\nu); \\ a_3 = \beta I_3\,[(\mu+\nu)A + \mu]\,\psi = Aq_1(1+r)\psi \text{ with } r = \frac{\mu}{\mu+\nu}\frac{1}{A}. \end{cases} \tag{11}$$

We would like to understand the stability of E_3 using Routh-Hurwitz's theorem.
We can immediately notice that $a_1, a_3 > 0$, therefore the first two Routh-Hurwitz conditions are satisfied.
Consequently, there remains to verify when the third condition is achieved, that is to say when $a_1a_2 - a_3 > 0$.
According to definitions of a_1, a_2, a_3 reported in (16), we can rewrite the third condition as it follows:

$$\begin{aligned} a_1a_2 - a_3 > 0 \quad &\Leftrightarrow \quad (A\psi + q_2)(A\psi q_2 + q_1) - Aq_1(1+r)\psi > 0 \\ &\Leftrightarrow \quad q_2A^2\psi^2 + A(q_2^2 - q_1r)\psi + q_1q_2 > 0. \end{aligned}$$

Therefore,

- if $q_2^2 - q_1 r \geq 0$ $\left(\Leftrightarrow \gamma \geq \tilde{\gamma} := p_3^2 \left[\frac{\mu\theta\beta I_3}{(\mu+\beta I_3)^2} - \alpha\right]\right)$, then all the terms of the expression $q_2 A^2\psi^2 + A(q_2^2 - q_1 r)\psi + q_1 q_2$ are positive (or at most one equal to zero) and so $a_1 a_2 - a_3 > 0$, which implies E_3 is LAS;

- if $q_2^2 - q_1 r < 0$, in some cases $a_1 a_2 - a_3 > 0$ but in other cases it could be negative.

Let us analyse this latter case in a deeper way.
The equation $a_1 a_2 - a_3 = q_2 A^2\psi^2 + A(q_2^2 - q_1 r)\psi + q_1 q_2 = 0$ has got the following determinant:

$$\Delta = A^2(q_2^2 - q_1 r)^2 - 4A^2 q_2^2 q_1.$$

$\longrightarrow$ If $\Delta < 0$ $\left(\Leftrightarrow \gamma > \hat{\gamma} := p_3^2 \left[\frac{\mu\theta\beta I_3}{(\mu+\beta I_3)(\mu+\beta I_3+2\sqrt{\beta I_3(\mu+\nu)})} - \alpha\right]\right)$,
then $segn(a_1 a_2 - a_3) = segn(q_2 A^2) > 0$, and so E_3 is still LAS.

But since $\tilde{\gamma} > \hat{\gamma}$, the two previous conditions on locally asimptotically stability can be summarized just considering the second one:
if $\gamma > \hat{\gamma}$, then E_3 is LAS. This proves point (A) of the theorem.
$\longrightarrow$ If $\Delta > 0$ ($\Leftrightarrow$ if $\gamma < \hat{\gamma}$), then the equation admits two positive solutions

$$u_1 = \frac{-(q_2^2 - q_1 r) - \sqrt{\Delta}}{2q_2 A^2}, \qquad u_2 = \frac{-(q_2^2 - q_1 r) + \sqrt{\Delta}}{2q_2 A^2}.$$

with $u_1 < u_2$.
Therefore, if $\psi \in (0, u_1) \cup (u_2, \infty)$, then $a_1 a_2 - a_3 > 0$ and so E_3 remains LAS; otherwise if $\psi \in (u_1, u_2)$, E_3 becomes *unstable*.

Point (B) of the theorem is nearly completely proved too.
There remains to understand the presence of oscillatority in the sense of Yakubovich in the unstable case.
We assume now to have a value of $\gamma < \hat{\gamma}$ such that E_3 is unstable.
Therefore, the system has three isolated, hyperbolic and unstable equilibria: E_1, E_2, E_3.
Consequently, hypotheses $H.1$ and $H.3$ of Yakubovich's theorem (see theorem (.8) in the Appendix) are achieved.
Furthermore, since the vector of the state variables $(S(t), I(t), p(t))$ has got $D := \left\{(S, I, p) \in \mathbb{R}^3_+ / S + I \leq 1, p \leq 1\right\}$ as definition set, all solutions of the system are bounded and so also hypothesis $H.2$ is satisfied.
In conclusion, thanks to Yakubovich's theorem, the system, in the unstable endemic regime, is oscillatory in the sense of Yakubovich.

The proof is now completed. □

As in the chapter about $I - model$, also here we can try and find a Hopf bifurcation parameter that allows to locally establish the presence of regular (periodic) oscillatority:

Corollary 0.4 (Hopf Bifurcation)**.** Let us refer to notations used in the theorem above.
Under appropriate conditions, ψ is a Hopf bifurcation parameter and u_1, u_2 are Hopf bifurcation critical values.

The proof is not reported because it is analogous to that one of the previous chapter.

0.13.5 Equilibria and their stability: summary

To better understand the full picture of $G - model$ equilibria and their stability, here it is a summary:

- A pure-vaccinator $DFE,\ E_1 = (0, 0, 1)$, always exists:
  if $\gamma > \gamma_1$, it is GAS,
  if $\gamma < \gamma_1$, it is *unstable*.
- If $\gamma < \gamma_1$, a $DFE,\ E_2 = (1 - p_2, 0, p_2)$, appears:
  if $\gamma > \gamma_c$, it is GAS,
  if $\gamma < \gamma_c$, it is *unstable*.
- If $\gamma < \gamma_c$, an $EE,\ E_3 = (R_0^{-1}, I_3, p_3)$, appears:
  it is LAS in some cases, but might also become *unstable*.

0.14 Possible eradication and Pure Vaccinator Equilibrium

As we can see there is a correspondence between the strength of public effort and the values of γ, in particular high levels of PHS intervention are linked to big values of γ.
Looking at the summary on $G - model$ equilibria and their stability, we can notice that public intervention gives a plausible mechanism for ELIMINATION equilibrium E_2 to be GLOBALLY ATTRACTIVE.

To better understand this, let us enter in a control perspective.

If the infection is endemic (we have values of γ that allow equilibrium E_3 to exist) and the public intervention is mild or absent, it is possible to increase the equilibrium coverage by increasing the public effort (increasing γ) in providing information about the benefits of vaccination. Suitable further increase in public effort can allow the equilibrium vaccine uptake to expand until the endemic state E_3 disappears by exchanging its stability with the DFE point E_2, thus achieving elimination. Further increases in γ yield further increase in vaccine uptake, until E_2 collapses into the PVE E_1. In particular, values of γ such that $\gamma > \gamma_c$ modulate the speed of elimination.

From this observations, not only it emerges that the public intervention gives a plausible mechanism towards eradication of pediatric infectious diseases, but even that it allows, when very strong, the PVE to be GLOBALLY ATTRACTIVE.

Therefore, clearly, $G-model$ improves $I-model$ in the direction of achieving disease eradication.

0.15 G-model equilibria compared with I-model equilibria

Looking, once more, at the summary on $G-model$ equilibria and their stability, it is clear that $G-model$ DOES NOT allow PURE NON VACCINATOR equilibria where none vaccinates.

Indeed, if we put $p = 0$ into system (9), from the equation of p', we have

$$p' = k\gamma \neq 0.$$

On the contrary, from the summary on $I-model$ equilibria and their stability, it emerges that $I - model$ has got two pure non vaccinator equilibria, that are $C_1 = (1, 0, 0)$ and $C_3 = (R_0^{-1}, \frac{\mu p_c}{\mu+\nu}, 0)$.

Therefore, we can infer that public intervention improves $I - model$ also in the sense that it always allows the establishment of some positive level of vaccine uptake.

0.16 Italian data on measles coverage and the interplay of public and private information

Let us recall Italian data on measles vaccine uptake observed in $1996-2008$ years:

- in 1996, measles coverage had a national average of $p^{1996} = 56\%$;
- in 2003, the first dose national coverage increased up to $p^{2003} = 78\%$;
- in 2008, it reached $p^{2008} = 90\%$.

Let us consider the same values of demo-epidemiological parameters used in simulations in the previous chapter:

$$\mu = \frac{1}{78}\ years^{-1},\ \nu = \frac{365}{7}\ years^{-1},\ R_0 = 15.$$

Furthermore, let us define parameters $\bar{\gamma}$ and $\bar{\alpha}$ as it follows:

$$\bar{\gamma} := \frac{\gamma}{\theta}, \quad \bar{\alpha} := \frac{\alpha}{\theta}.$$

From system (10), which describes the couples (I_3, p_3) of equilibrium E_3, we can infer that

$$I_3 = \bar{\alpha} p_3 - \frac{\bar{\gamma}}{p_3},$$

where p_3 is the positive solution of the following second order algebraic equation in p:

$$[\bar{\alpha}(\mu+\nu)+\mu]\, p^2 - \mu p_c p - (\mu+\nu)\bar{\gamma} = 0. \tag{12}$$

Given the impossibility of fitting behavioral parameters due to the paucity of data, we can attempt at least to disentangle the relative role of private against public information by using the few Italian data on measles coverage reported above.

We hypothesize that:
(a) the "low" uptake of vaccine against measles observed in 1996 (56%) reflects the steady state of a voluntary immunization program based on $I-model$;
(b) the sharp increase in uptake observed during $1996-2008$ mirrors, at least crudely, a new steady state situation, implied by the initiation of a public

program which rapidly raised γ from zero up to a positive value, on the assumption that the imitation-related parameters remained constant during the same period.

Under these assumptions, we can determine the relationships between the main behavioral parameters (α, γ, θ) as it follows.
As hypothesized above (assumption (a)), the routine uptake of vaccine against measles $p^{1996} = 0.56$, observed at 1996, is taken as the equilibrium uptake of an underlying $I - model$.
Therefore, putting $\bar{\gamma} = 0$ ($I-model$ case) and $p = p_3 = p^{1996}$ in equation (12), we can find the corresponding value of $\bar{\alpha}$:

$$\bar{\alpha}^{1996} = \frac{\mu(p_c - p^{1996})}{(\mu + \nu)p^{1996}} = 1.638 \times 10^{-4},$$

which implies $\frac{\theta}{\alpha} = \frac{1}{\bar{\alpha}^{1996}} = 6105$.
This large disproportion between θ (the perceived probability of suffering a serious illness as consequence of infection) and α (the perceived probability of suffering a VSE as consequence of vaccination) comes from the hypothesis that the perceived risk of infection is prevalence-dependent.
Note that achieving the value $p^{2008} = 0.90$ of routine vaccine uptake against measles observed in 2008 as equilibrium coverage would require, under imitation dynamics only, a 20−fold decline in $\bar{\alpha}$, up to $\bar{\alpha}^{2008} = 0.091 \times 10^{-4}$ (as above, this comes from putting $\bar{\gamma} = 0$ and $p = p_3 = p^{2008}$ in equation (12)), that implies $\frac{\theta}{\alpha} = 109890$.
This large drop, which corresponds to a significantly growth of the perceived probability of suffering a serious illness with respect to the perceived probability of suffering a VSE, suggests that the marked increase in vaccine uptake observed in Italy in such a short period of time is unlikely to have been achieved by changes in costs perceived during spontaneous contacts between individuals alone.
Therefore, let us determine $\bar{\gamma}$ from equation (12), on the assumption (b) that p^{2008} represents the endemic uptake p_3 of $G - model$ and that $\bar{\alpha}$ remained unaltered during $1996 - 2008$:

$$\bar{\gamma}^{2008} = \frac{\left[\bar{\alpha}^{1996}(\mu + \nu) + \mu\right](p^{2008})^2 - \mu p_c p^{2008}}{\mu + \nu} = 1.253 \times 10^{-4}.$$

This implies $\frac{\gamma}{\alpha} = \frac{\bar{\gamma}^{2008}}{\bar{\alpha}^{1996}} = 0.765$ and hence that $\frac{\gamma}{\alpha} < p_c^2 = (1 - R_0^{-1})^2 = 0.871$, that is to say the system is in its endemic region.
In order to achieve elimination it would be required that $\frac{\gamma}{\alpha} > p_c^2 = 0.871$, as already stated.

0.17 Simulations

To better understand the role played by the PHS on vaccination programs, I made some specific simulations using MATLAB.
First of all, note that we can reparametrize the equation, in system (9), for the dynamics of the vaccinated proportion $p(t)$, as it follows:

$$p' = k\theta(1-p)\left[(I-\bar{\alpha}p)p+\bar{\gamma}\right].$$

Therefore, each couple of values $(\bar{\alpha},\bar{\gamma})$ are compatible with a wide variety of dynamic endemic regimes, depending on the product $k\theta$.
Consequently, in each simulation, I choosed a proper value of the product $k\theta$ in order to guarantee an oscillatory endemic regime for both $I-model$ and $G-model$.
In the following simulations, the Effective Reproduction Number $Re(t)$ is used instead of the state variable $S(t)$.

0.17.1 Dynamics of different models for vaccination behavior with and without public intervention

This first simulation compares, over a time horizon of 150 years, the predicted dynamics of $G-model$ and $I-model$ with endemic vaccine uptake equal to the value observed in Italy in 2008 ($p_3 = p^{2008} = 0.90$), together with the $SIR-model$ with mandatory vaccination set to $p_{SIR} = p^{2008} = 0.90$.
Initial condition. For this simulation I used the following initial condition:

$$(S(0), I(0), p(0)) = (1.04/R_0, 0.82\times 10^{-5}, 0.95).$$

Choice of the value of the product $k\theta$.

- We have an $I-model$ with endemic coverage $p_3 = p^{2008} = 0.90$ to which corresponds, as we have already computed, $\bar{\alpha}^{2008} = 0.091\times 10^{-4}$. Therefore, through observations coming from the previous chapter, we have immediately that, in order to allow an oscillatory endemic regime, in this case, $k\theta$ should range between 869.166 and 5.732×10^8.

- We have a $G-model$ with endemic coverage $p_3 = p^{2008} = 0.90$ to which corresponds, as already computed, $\bar{\gamma}^{2008} = 1.253\times 10^{-4}$.

  In order to find a proper range for the product $k\theta$ in this latter case, we should look at the third Routh-Hurwitz condition reported into the proof of the theorem about E_3 stability.

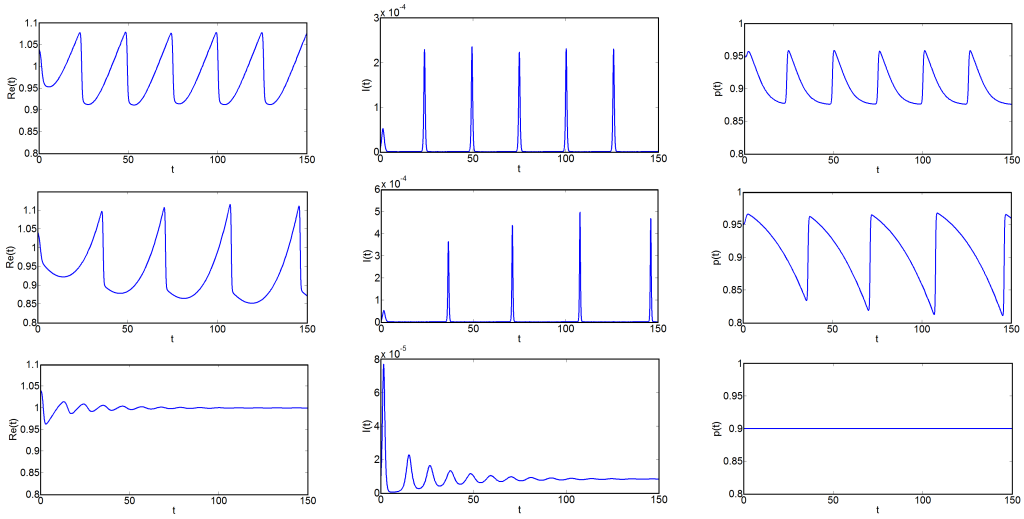

Figure 5: Dynamics of $Re(t)$ (left column), $I(t)$ (central column) and $p(t)$ (right column) for different models: $G-model$ with endemic coverage $p_3 = p^{2008} = 0.90$ (top row), $I-model$ with endemic coverage $p_3 = p^{2008} = 0.90$ (central row) and $SIR-model$ with mandatory vaccination set to $p_{SIR} = p^{2008} = 0.90$ (bottom row).

We can read the equation $q_2 A^2\psi^2 + A(q_2^2 - q_1 r)\psi + q_1 q_2 = 0$, which defines the third condition, as a second degree equation with respect to $A\psi$ instead of ψ alone, that is to say

$$q_2(A\psi)^2 + (q_2^2 - q_1 r)(A\psi) + q_1 q_2 = 0.$$

This equation admits solutions

$$(A\psi)_{1,2} = \frac{-(q_2^2 - q_1 r) \mp \sqrt{\frac{\Delta}{A^2}}}{2q_2},$$

where $\Delta = (q_2^2 - q_1 r)^2 A^2 - 4q_1 q_2^2 A^2$.

We can easily compute these two specific values, remembering the definitions of the quatities that appear in their expressions:

$$I_3 := \frac{\mu(p_c - p_3)}{\mu + \nu},\ q_1 := R_0(\mu+\nu)^2 I_3,\ q_2 := \mu + R_0(\mu+\nu)I_3,$$

$$A := \left(\bar{\alpha} + \frac{\bar{\gamma}}{p_3^2}\right)\ and\ r := \frac{\mu}{\mu+\nu}\frac{1}{A}.$$

Once we have achieved the numerical values of $(A\psi)_1$ and $(A\psi)_2$, it remains to use the definition of ψ ($\psi := k\theta p_3(1-p_3)$), so that we can infer

$$(k\theta)_{1,2} = \frac{(A\psi)_{1,2}}{Ap_3(1-p_3)}.$$

In particular, I obtained

$$(k\theta)_1 = 872.136,\ (k\theta)_2 = 4.666 \times 10^5.$$

Therefore, to allow an oscillatory endemic regime in this case, $k\theta$ should range between 872.136 and 4.666×10^5.

- We have also a $SIR-model$ with mandatory vaccination set to $p_{SIR} = p^{2008} = 0.90$. Since $p_c = 1 - R_0^{-1} = 0.93 > 0.90 = p_{SIR}$, therefore, as we have already seen in the chapter about $SIR-model$, the model is in its stable endemic regime, irrespective to the value of the product $k\theta$.

In conclusion, in order to guarantee an oscillatory endemic regime for both $I-$ and $G-model$, $k\theta$ should stay in the following window of values:

$$k\theta \in (872.136, 4.666 \times 10^5).$$

In this simulation I choosed a value of $k\theta$, inside that window, equal to 6500.

Comments. Let us look at figure (5) for a complete picture of the situation and at figure (6) for specific details.
$SIR-model$ is in its stable endemic regime. This emerges from the bottom row of figure (5), which shows $SIR-model$ traditional damped oscillations. Looking at figure (5), a comparison between $I-model$ and $G-model$ arises spontaneously:

- $I-model$ shows inter-epidemic period around 40 years, while with $G-model$ the period of this oscillations is much shorter, about 25 years (see figure (6)).

  This could be explained by the fact that in correspondence of an epidemic outbreak, PHS intervention try and increase vaccine uptake, against its natural fall in the presence of imitation dynamics only. This leads to a corresponding decrease in the fraction of susceptible until the end of the epidemic outbreak.

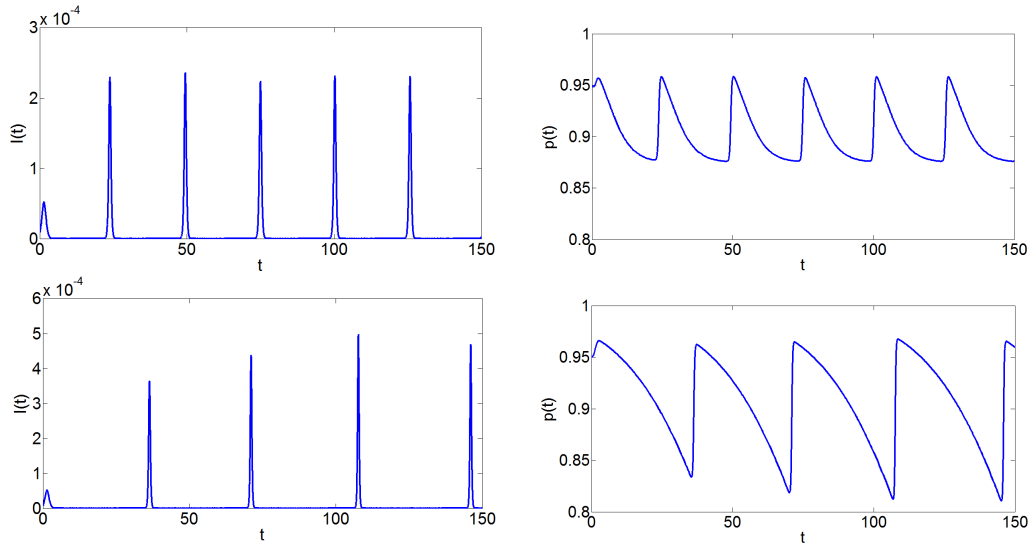

Figure 6: Detail on the dynamics of $I(t)$ (left column) and $p(t)$ (right column) for $G-model$ with endemic coverage $p_3 = p^{2008} = 0.90$ (first row) and $I-model$ with endemic coverage $p_3 = p^{2008} = 0.90$ (second row).

- Public intervention has a strong stabilising effect on the oscillations of vaccine uptake (see figure (6)):

  1. it reduces the amplitude of oscillations, which are confined between 87% and 96% (against the amplitude confined between 80% and 97% with $I-model$).

  2. It achieves a higher average in vaccine uptake than the corresponding model with imitation dynamics alone.

0.17.2 Dynamics of $G-model$ triggered by different levels of public intervention

This second simulation illustrates the impact, over a time span of 80 years, of different levels of public intervention as represented through increasing values of $\bar{\gamma}$, aiming to achieve the following targets of vaccine uptake:

- endemic equilibrium coverage $p_3 = p^{2003} = 0.78$, given by the measles coverage recorded in Italy in 2003 after the first big wave of public intervention;

- endemic equilibrium coverage $p_3 = p^{2008} = 0.90$, given by the measles coverage recorded in Italy in 2008;

- elimination coverage $p_2 = 0.95$, which is the WHO target for measles elimination;

- elimination with everyone vaccinating (the PVE) $p_1 = p_2 = 1$.

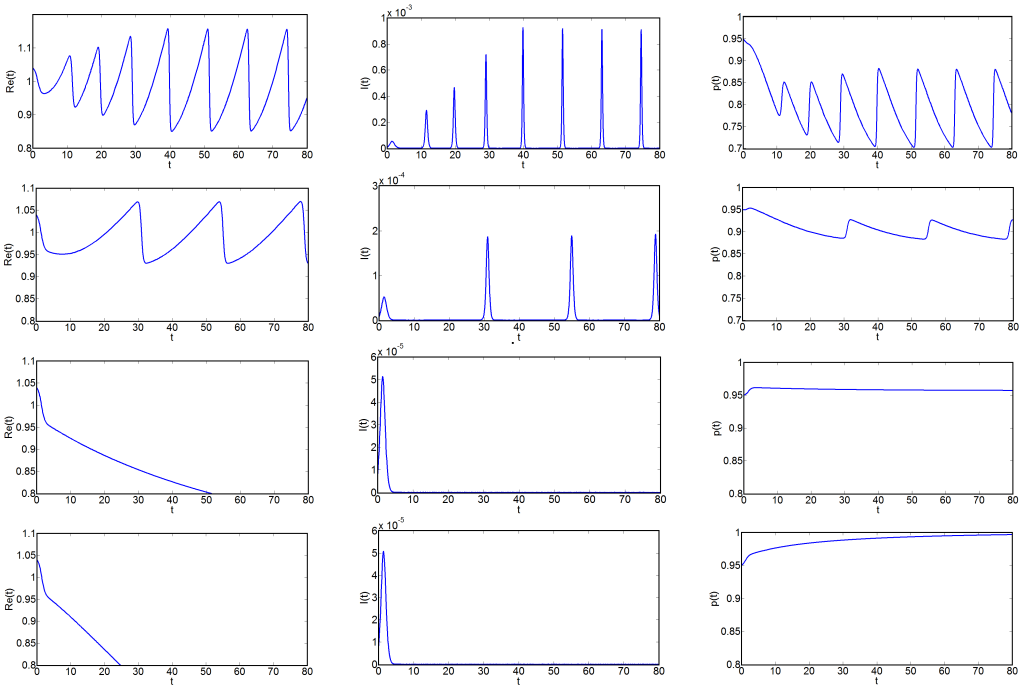

Figure 7: $G - model$ and the dynamics of $Re(t)$ (left column), $I(t)$ (central column) and $p(t)$ (right column) for different levels of public intervention: $\bar{\gamma}$ set to achieve endemic coverage $p_3 = p^{2003} = 0.78$ (top row), $\bar{\gamma}$ set to achieve endemic coverage $p_3 = p^{2008} = 0.90$ (second row), $\bar{\gamma}$ set to achieve elimination coverage $p_2 = 0.95$ (third row) and $\bar{\gamma}$ set to achieve the PVE $p_2 = p_1 = 1$ (bottom row).

Initial condition. For this simulation I used the following initial condition:

$$(S(0), I(0), p(0)) = (1.04/R_0, 0.82 \times 10^{-5}, 0.95).$$

Choice of the value of the product $k\theta$.
Let us consider $\bar{\alpha}$ fixed at the value $\bar{\alpha}^{1996} = 1.638 \times 10^{-4}$.

- We have a $G - model$ with researched endemic coverage $p_3 = p^{2003} = 0.78$, to which corresponds $\bar{\gamma}^{2003} = 0.703 \times 10^{-4}$ (this value can be inferred using, once more, equation (12) satisfied by p_3).

Therefore, with passages similar to what we have already seen in the first simulation, I found that, in order to allow an oscillatory endemic regime, in this case, $k\theta$ should range between 1005.8 and 6.654×10^5.

- We have a $G - model$ with researched endemic coverage $p_3 = p^{2008} = 0.90$, to which corresponds, as already computed, $\bar{\gamma}^{2008} = 1.253 \times 10^{-4}$.

  Therefore, as we have already found, in order to allow an oscillatory endemic regime, in this case, $k\theta$ should range between 872.136 and 4.666×10^5.

- We have a $G - model$ with researched elimination coverage $p_2 = 0.95$.

  Let us report here the condition which guarantees the existence and the global stability of the $DFE\ E_2$:

  $$\alpha p_c^2 := \gamma_c < \gamma < \gamma_1 = \alpha.$$

  Dividing for θ all the members of the chain of inequalities above, we have

  $$\bar{\alpha} p_c^2 < \bar{\gamma} < \bar{\alpha}.$$

  But, $\bar{\alpha} p_c^2 = 1.417 \times 10^{-4}$ and $\bar{\alpha} = \bar{\alpha}^{1996} = 1.638 \times 10^{-4}$.

  Therefore, in order to achieve eradication, I choosed a value of $\bar{\gamma}$, inside that range, equal to 1.5×10^{-4}.

  Note that, in this case, the model is in its stable disease free regime, irrespective to the value of the product $k\theta$.

- We have a $G - model$ with researched elimination coverage with everyone vaccinating $p_1 = p_2 = 1$.

  The condition which guarantees the existence and the global stability of the $DFE\ E_1$ is:

  $$\gamma > \gamma_1 = \alpha,$$

  that can be read, dividing for θ, as

  $$\bar{\gamma} > \bar{\alpha}.$$

  Therefore, in order to achieve eradication with everyone vaccinating, I choosed a value of $\bar{\gamma}$, greater than 1.638×10^{-4}, equal to 1.7×10^{-4}.

  Note that, also in this case, the model is in its stable disease free regime with everyone vaccinating, irrespective to the value of the product $k\theta$.

In conclusion, in order to allow an oscillatory endemic regime for both the first two $G-model$ cases, $k\theta$ should stay in the following window of values:

$$k\theta \in (1005.8, 4.666 \times 10^5).$$

In this simulation I choosed a value of $k\theta$, inside that window, equal to 3000.

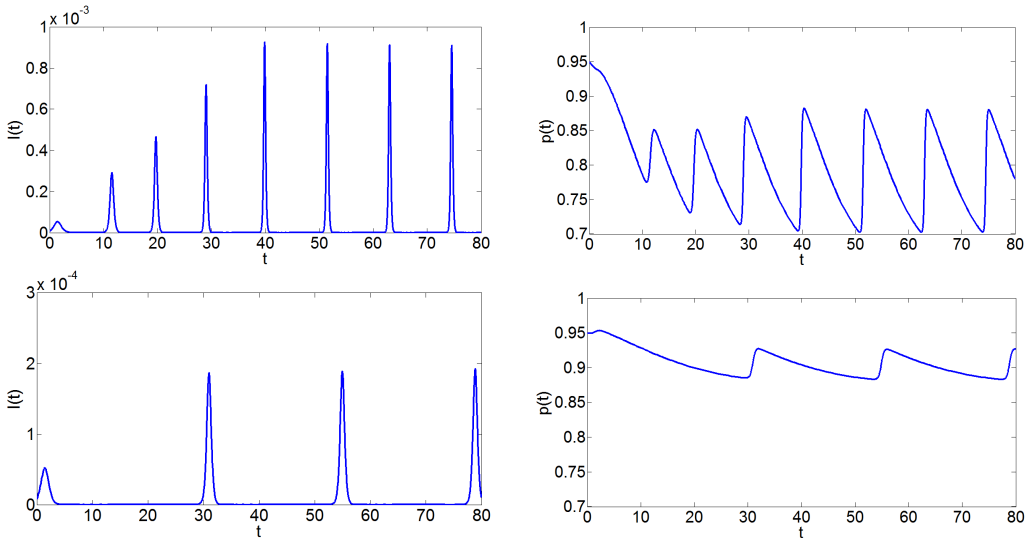

Figure 8: Detail on the dynamics of $I(t)$ (left column) and $p(t)$ (right column) for $G-model$ with $\bar{\gamma}$ set to achieve endemic coverage $p_3 = p^{2003} = 0.78$ (first row) and $G-model$ with $\bar{\gamma}$ set to achieve endemic coverage $p_3 = p^{2008} = 0.90$ (second row).

Comments. Let us look at figure (7) for a complete picture of the situation and at figures (8) and (9) for more details.

- The first two scenarios (see figure (8)) predict disease persistence and confirm the stabilising role played by public information.

  Note that the amplitude of oscillations in vaccine uptake are confined between 70% and 90% in the first case and between 85% and 95% in the second one, in which PHS intervention (respectively the value of $\bar{\gamma}$) is higher.

  Furthermore, note that the vaccinated proportion is always maintained at high values, expecially in the second case.

- The last two scenarios (see figure (9)) yield elimination and they show the interesting fact that, though public intervention is unable to avoid large initial epidemic due to the large initial susceptible fraction, it is

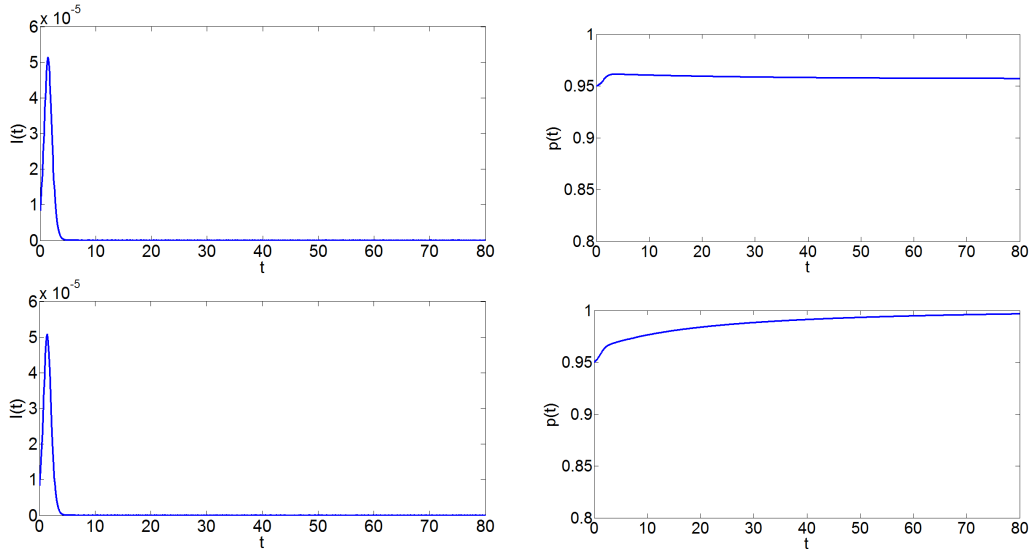

Figure 9: Detail on the dynamics of $I(t)$ (left column) and $p(t)$ (right column) for $G-model$ with $\bar{\gamma}$ set to achieve elimination coverage $p_2 = 0.95$ (first row) and $G - model$ with $\bar{\gamma}$ set to achieve the PVE $p_2 = p_1 = 1$ (second row).

subsequently able to avoid the drop in uptake, that would unavoidably occur in an $I - model$ as a consequence of the large number of vaccines administered.

The large initial epidemic creates a phase where the perceived risk of disease is high thereby also speeding up the private component of vaccination, which in this case works synergically with the public one in accelerating disease elimination.

0.17.3 Dynamics of measles coverage in Italy between 1996 and 2040 years

To investigate whether $G - model$ explains the growth in uptake of vaccine against measles in Italy during $1996 - 2008$ years, we study the response of model behavior to changes in $k\theta$, conditionally on the values determined for $\bar{\alpha}, \bar{\gamma}$.
Here the purpose is to identify combinations of $\bar{\alpha}, \bar{\gamma}, k\theta$ compliant with patterns of vaccine uptake observed in Italy in $1996 - 2008$ and compare predictions (until 2040 year) provided by the proposed $G - model$ with those based on $I - model$.
We consider, for four increasing values of $k\theta$, the behavior of vaccine uptake in four alternative models:

- $I - model$ with $\bar{\alpha}$ set to allow an endemic vaccine uptake p_3 equal to the level of 0.56 observed in Italy prior to 1996,

- $I - model$ with $\bar{\alpha}$ reduced to allow an endemic vaccine uptake p_3 of 90% as observed in Italy in 2008,

- $G-model$ with $\bar{\alpha}$ set at the pre-1996 level and $\bar{\gamma}$ set to allow an endemic vaccine uptake p_3 of 90%,

- $G - model$ with $\bar{\gamma}$ allowing an elimination coverage p_2 of 95%.

The four models are all initialised at $t = 1996$, since we hypothesize that prior to 1996 vaccine uptake was at the steady state of an $I - model$ with coverage of 56%.

Initial condition. For this simulation I used the following initial condition:

$$(S(0), I(0), p(0)) = (1/R_0, 9.2 \times 10^{-5}, 0.56).$$

Choice of the four values of $k\theta$.

- We have an $I - model$ with researched endemic coverage $p_3 = p^{1996} = 0.56$, to which corresponds $\bar{\alpha}^{1996} = 1.638 \times 10^{-4}$.

  Therefore, with passages similar to what we have already seen, I found that, in order to allow an oscillatory endemic regime, in this case $k\theta$ should range between 1399.5 and 1.642×10^6.

- We have an $I - model$ with researched endemic coverage $p_3 = p^{2008} = 0.90$, to which corresponds, as already computed, $\bar{\alpha}^{2008} = 0.091 \times 10^{-4}$ and the oscillatority range $(869.166, 5.732 \times 10^8)$ for the product $k\theta$.

- We have a $G - model$ with researched endemic coverage $p_3 = p^{2008} = 0.90$, to which corresponds, as already computed, $\bar{\gamma}^{2008} = 1.253 \times 10^{-4}$ and the oscillatority range $(872.136, 4.666 \times 10^5)$ for the product $k\theta$.

- We have a $G - model$ with researched elimination coverage $p_2 = 0.95$. I associated to this case the same value of $\bar{\gamma}$ I computed in the previous simulation, that is $\bar{\gamma} = 1.5 \times 10^{-4}$.

  This latter model is in its stable regime, irrespective to the value of the product $k\theta$.

In conclusion, in order to allow an oscillatory endemic regime in all cases (both for $I-$ and $G-models$) reported above, the product $k\theta$ should be in the following window of values:

$$k\theta \in (1399.5, 4.666 \times 10^5).$$

The four increasing values of $k\theta$, inside the interval above, I choosed for this simulation are:

$$k\theta = 1500, 2000, 3000, 4000.$$

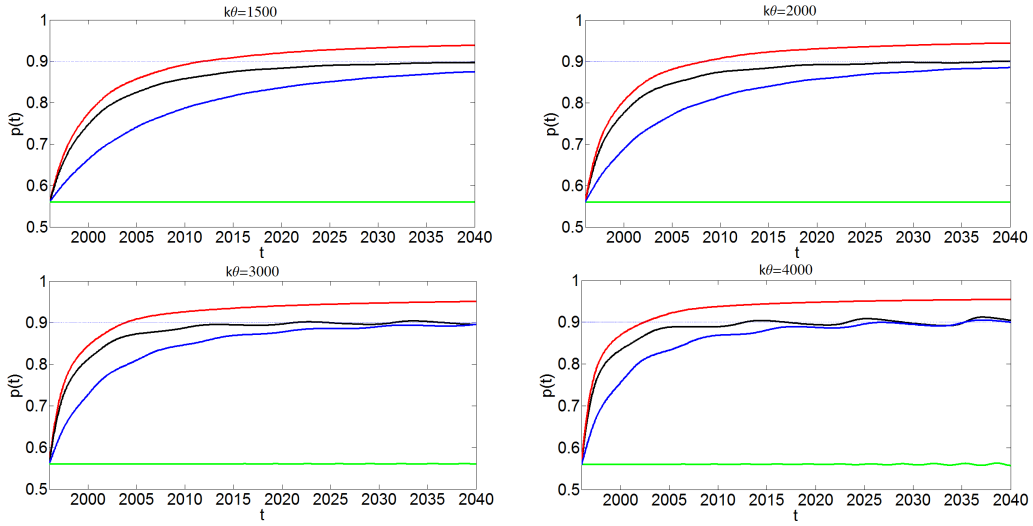

Figure 10: Four panels for four different values of $k\theta$: $1500, 2000, 3000, 4000$. Each panel predicts $p(t)$ dynamics for four different models: $I-model$ with $\bar{\alpha}$ set to allow $p_3 = p^{1996} = 0.56$ (green line), $I-model$ with $\bar{\alpha}$ set to allow $p_3 = p^{2008} = 0.90$ (blue line), $G-model$ with $\bar{\gamma}$ set to allow $p_3 = p^{2008} = 0.90$ (black line), $G-model$ with $\bar{\gamma}$ set to allow $p_2 = 0.95$ (red line). A dotted line at level 0.90 is also added for reference.

Comments. Looking at figure (10), we can infer that

- $I-model$ with $\bar{\alpha}$ set to allow $p_3 = 0.56$ (green line) continues to follow its equilibrium pattern (stationary or oscillatory). On the other hand, the other models predict a sharp increase in vaccine uptake (note the increase is monotonic for values of $k\theta$ below a threshold and oscillatory thereafter).

- In $G-model$ vaccine uptake grows much faster than the $I-model$, regardless of the chosen value of $k\theta$, although the imitation model is

now evolving under an implausibly large value of $\bar{\alpha}$, which is 20−fold lower compared to the pre-1996 period, thereby implying an implausible decrease in relative perceived risk of vaccine side effects compared to the past. Thus $G-model$ seems to account for the observed growth in measles uptake much better than $I-model$.

- In particular, the $G-model$ with equilibrium uptake $p_2 = 0.95$ (red line) allows, expecially for $k\theta = 2000$, to closely reproduce the observed growth of measles vaccine uptake in $1996-2008$. We also note that the same result can only be approached in $I-model$ by implausibly large $k\theta$ values yielding huge, unreasonable oscillations.

Conclusions

Both basic $SIR - models$ for vaccine preventable infections and $I - model$, where vaccination choices are voluntary and based upon an imitation mechanism, are expanded into another SIR transmission model with voluntary immunization.
The ensuing mathematical model considers of central importance the role played by human behavior in determining vaccination outcome and it suggests how public intervention can offset the pessimistic conclusions based on models with imitation dynamics alone.
In particular, the intervention of the PHS is shown to always play a stabilising role able to reduce the strength of imitation-induced oscillations in vaccine uptake, always allow the establishment of some positive level of vaccine uptake, remove the "elimination impossible" result and even make, when sufficiently strong, the DFE where everyone vaccinate globally attractive.
Furthermore, from the last proposed simulation, it emerges how $G - model$ seems to offer a much more plausible behavior-based explanation of the rapid increase in measles vaccine uptake, observed in Italy in $1996 - 2008$ years, than models based on imitation alone.
Therefore, all these results illustrate how public intervention might be the main provider of information on diseases and vaccines able to ensure a rapid increase in vaccine uptake in situations where individual choices have caused policy stagnation.

Finally, it is worth noting that the results reached in this thesis are based on the assumption of a linear perceived cost of suffering serious diseases: $\rho_I(t) = r(I(t)) = \theta I$, with θ a positive constant. This assumption come from considering the first simpler form for $\rho_I(t)$ in order to concentrate the thesis not on computations themselves, but on a suitable comparison of what happens to the dynamics of vaccine uptake if information on the disease come from private exchange of opinions alone or from public channels too.
Actually, in reality, there are some parents that decide to vaccinate their children, even though the fraction of infectives is zero.

Therefore, it was more appropriate to consider an affine form, such as

$$\rho_I(t) = r(I(t)) = \theta I + \theta_0,$$

with θ, θ_0 positive constants.
In this case, even if in absence of infectives, there is a constant non zero perceived cost of suffering serious diseases θ_0.
The following last chapter contains the summaries of $I-model$ and $G-model$ equilibria in the affine case.

Perceived cost of suffering serious diseases: affine case

0.18 $I - model$: affine case

In what follows there is a summary on $I - model$ equilibria that comes from considering a perceived cost of suffering serious diseases of the form

$$\rho_I(t) = r(I(t)) = \theta I + \theta_0,$$

with θ, θ_0 positive constants.

Equilibria and their stability:

- $C_1 = (1, 0, 0)$ always exists; it is always unstable.
- $C_2 = (0, 0, 1)$ always exists; if $\theta_0 > \alpha$ it is GAS, otherwise it is unstable.
- If $\theta_0 < \alpha$, $C_5 = (1 - p_5, 0, p_5)$, with $p_5 = \frac{\theta_0}{\alpha}$, appears; when it exists, it is always unstable.
- $C_3 = (R_0^{-1}, \frac{\mu p_c}{\mu+\nu}, 0)$ always exists; it is always unstable.
- If $\theta_0 < \alpha p_c$, $\tilde{C_4} = (R_0^{-1}, \tilde{I}_4, \frac{\theta \tilde{I}_4 + \theta_0}{\alpha})$, with $\tilde{I}_4 = \frac{p_c - \frac{\theta_0}{\alpha}}{\frac{\theta}{\alpha} + \frac{\nu}{\mu} + 1}$, appears; it is LAS in some cases, but it might also be unstable.

Comments:
As we can see, if $\theta_0 > \alpha$ the pure-vaccinator DFE C_2 is GAS, consequently with the affine case we are able to achieve disease eradication with $I - model$ too.
Compared to the linear case, the summary above contains one more DFE C_5, even if it is always unstable.

Furthermore, in the linear case the EE C_4 always exists, while here the EE $\tilde{C}_4$ exists if and only if $\theta_0 < \alpha p_c$.
Therefore, the affine case clearly improves the linear one.
Furthermore, it is worth noting that with the affine form we land to analogous results reached considering public intervention.
Thus, in order to achieve disease eradication it is necessary to mantain vaccine uptake at values higher than proper thresholds, but it does not bother if this is obtained thanks to public intervention or thanks to those parents which decide by themselves, without being persuaded by PHS, to immunize their children even if the fraction of infectives is zero.

0.19 $G-model$: affine case

In what follows there is a summary on $G-model$ equilibria that comes from considering a perceived cost of suffering serious diseases of the form

$$\rho_I(t) = r(I(t)) = \theta I + \theta_0,$$

with θ, θ_0 positive constants.

Equilibria and their stability:

- $E_1 = (0, 0, 1)$ always exists; if $\gamma > \alpha - \theta_0$ it is GAS, otherwise it is unstable.
- If $\gamma < \alpha - \theta_0$, $\tilde{E}_2 = (1 - \tilde{p_2}, 0, \tilde{p_2})$, with $\tilde{p_2} = \frac{\theta_0 + \sqrt{\theta_0^2 + 4\alpha\gamma}}{2\alpha}$, appears; it is always LAS.
- If $\gamma < \alpha p_c^2 - 2\theta_0 p_c$, $\tilde{E}_3 = (R_0^{-1}, \tilde{I}_3, \tilde{p_3})$, with the couple $(\tilde{I}_3, \tilde{p_3})$ satisfying the following system

$$\begin{cases} I = \dfrac{\mu}{\mu + \nu}(p_c - p) \\ I = -\dfrac{\gamma}{\theta p} + \dfrac{\alpha p}{\theta} - \dfrac{\theta_0}{\theta}, \end{cases}$$

  appears; it is LAS in some cases, but it might also be unstable.

Comments:
As we can see, the DFE $\tilde{E}_2$ is always LAS, therefore with the affine case we are able to achieve disease eradication independently of the level of public intervention.

Furthermore, the linear threshold $\gamma_1 = \alpha$ corresponds here to the smaller one $\alpha - \theta_0$. Consequently, a lower level of public intervention is needed in order to have the pure-vaccinator DFE E_1 globally attractive.
Also in the $G - model$, the affine case results clearly to be an improvement of the linear one.

Routh-Hurwitz conditions

This appendix refers to "Appendix B: Routh-Hurwitz conditions, Jury conditions, Descartes' rule of signs and exact solutions of a cubic" of book [8].

Linear stability of systems of ordinary differential equations is determined by the roots of a polynomial.
The stability analysis involves linear systems of the vector form

$$\frac{dx}{dt} = Ax \tag{13}$$

where A is the matrix of the linearized nonlinear dynamical system: it is the Jacobian matrix about the steady state.
Solutions are obtained by setting

$$x = x_0 \exp(\lambda t)$$

in (13), where x_0 is a constant vector and the eigenvalues λ are the roots of the characteristic polynomial

$$\det(A - \lambda Id) = 0.$$

The solution $x = 0$ is locally asymptotically stable if all the roots λ of the characteristic polynomial lie in the left-hand complex plane, that is $Re\lambda < 0$ for all roots.
The theorem below is a powerfull method to derive the local stability of an equilibrium point, of a system of order n, with the following corresponding characteristic polynomial

$$P(\lambda) = \lambda^n + a_1\lambda^{n-1} + \cdots + a_{n-1}\lambda + a_n.$$

Theorem .5 (Routh-Hurwitz's theorem)**.** Given the polynomial

$$P(\lambda) = \lambda^n + a_1\lambda^{n-1} + \cdots + a_{n-1}\lambda + a_n,$$

with $a_i \in \mathbb{R},\ i = 1, \ldots, n,\ a_n \neq 0$.

Define the n Hurwitz matrices as it follows ($a_j = 0$ if $j > k$):

$$H_1 := [a_1], H_2 := \begin{bmatrix} a_1 & a_3 \\ 1 & a_2 \end{bmatrix}, H_k := \begin{bmatrix} a_1 & a_3 & \cdots & \cdots \\ 1 & a_2 & a_4 & \cdots \\ 0 & a_1 & a_3 & \cdots \\ 0 & 1 & a_2 & \cdots \\ \vdots & \ddots & \vdots & \\ 0 & 0 & \cdots & a_k \end{bmatrix}, \ k = 3, \cdots, n.$$

All the roots of $P(\lambda)$ are negative or have negative real part if and only if the determinants of all Hurwitz matrices are positive ($detH_k > 0, \ k = 1, \cdots, n$).

As an application, the cubic polynomial

$$P(\lambda) = \lambda^3 + a_1\lambda^2 + a_2\lambda + a_3,$$

has all the roots λ negative or with negative real part if and only if

$$\det [a_1] > 0, \det \begin{bmatrix} a_1 & a_3 \\ 1 & a_2 \end{bmatrix} > 0, \det \begin{bmatrix} a_1 & a_3 & 0 \\ 1 & a_2 & 0 \\ 0 & a_1 & a_3 \end{bmatrix} > 0,$$

that is, if and only if the following three conditions are simultaneously satisfied:

$$a_1 > 0, \ a_1a_2 - a_3 > 0, \ a_3 > 0.$$

Oscillatority in the sense of Yakubovich

This appendix refers to Chapter 3 of book [9] and to the article [6] of A. L. Fradkov and A. Y. Pogromsky.

We can say that some process is oscillatory if it does not approach any definite constant value as time goes on, but it changes its value permanently without diverging.
A convenient definition of oscillatority was introduced by V.A.Yakubovich in 1973.
Let us consider the following nonlinear dynamical system

$$\frac{dx}{dt} = F(x), \tag{14}$$

with $x(t) \in \mathbb{R}^n$ and F such that the system is forward complete, which means for all initial conditions its solutions exist for all time.

Definition .1 (Lagrange stable systems)**.**
System (14) is *Lagrange stable* if each solution of (14) is bounded.

Definition .2 (Oscillatority in the sense of Yakubovich)**.**
System (14) is oscillatory in the sense of Yakubovich ($Y - oscillatory$) if it is *Lagrange stable* and, for almost all initial conditions, for at least one component $x_i(t)$ of the corresponding vector solution $x(t)$ we have

$$\liminf_{t\to\infty} x_i(t) < \limsup_{t\to\infty} x_i(t).$$

In what follows, it is given a theorem which allows to detect $Y - oscillatority$ in nonlinear dynamical systems.

Definition .3.
System (14) is $\mathcal{L} - dissipative$ if there exists a constant $R > 0$ such that $\limsup_{t\to\infty} |x(t)| \leq R$ for all initial conditions.

This means that there exists a ball of radius R such that for any solution $x(t)$ there exists a time constant t_1 such that for all $t \geq t_1$ and for any $\epsilon > 0$ we have $|x(t)| \leq R$.
Obviously, the ball can be replaced by any compact set in R^n.
Note that all solutions of an $\mathcal{L} - dissipative$ system are bounded.
Therefore, any $\mathcal{L} - dissipative$ system is *Lagrange stable*.

Theorem .6 (Yakubovich's theorem)**.** Assume that

H.1 system (14) has only isolated equilibria $x_j,\ j = 1, 2, \cdots$;

H.2 system (14) is $\mathcal{L} - dissipative$;

H.3 $x_j,\ j = 1, 2, \cdots$ are hyperbolic points and each Jacobian matrix $J_{|x_j} = \frac{\partial F}{\partial x}(x_j)$ has at least one eigenvalue with positive real part.

Then system (14) is $Y - oscillatory$.

This theorem follows from Hartman-Grobman theorem (see theorem 7.1 of chapter 7 of book [10]). Here it is reported only its statement, without proof:

Theorem .7 (Hartman-Grobman theorem)**.**
Let $\bar{x}$ be an equilibrium of system (14). If the corresponding Jacobian matrix $J_{|\bar{x}}$ has no zero or purely immaginary eigenvalues, then there is a homeomorphism g defined on some neighborhood U of $\bar{x}$ in R^n locally taking orbits of the nonlinear flow ϕ_t of system (14) to those of the linear flow $\exp(tJ_{|\bar{x}})$ of system $\eta' = J_{|\bar{x}}\eta$.
The homeomorphism preserves the qualitative characteristics of nonlinear orbits.

Proof of theorem (.8).
According to the definition of $Y - oscillatority$, we have to show that the system is *Lagrange stable* and that, for almost all initial conditions, for at least one component $x_i(t)$ of the corresponding solution vector $x(t)$, the following inequality holds:

$$\liminf_{t\to\infty} x_i(t) < \limsup_{t\to\infty} x_i(t).$$

Firstly, we can immediately see that, as already observed, hypothesis $H.2$ makes system (14) *Lagrange stable*.
Then, thanks to the fact, coming from hypothesis $H.3$, that the system has only hyperbolic equilibria, we can apply Hartman-Grobman theorem to each equilibrium point of system (14).

Therefore, for each x_j, there is a homeomorphism g_j defined on some neighborhood U_j of x_j in R^n locally taking orbits of the nonlinear flow ϕ_t of system (14) to those of the linear flow $\exp(tJ_{|x_j})$ of system $\eta_j' = J_{|x_j}\eta_j$.
Note that, thanks to hypothesis $H.1$, we can assume that $U_j,\ j = 1, 2, \cdots$ are disjoint.
But, for the well-known theory on linear dynamical systems, since each Jacobian matrix $J_{|x_j} = \frac{\partial F}{\partial x}(x_j)$ has at least one eigenvalue with positive real part (look at hypothesis $H.3$), we can say that for all j, for at least one component $k(j)$ of the corresponding linear solution $\eta_j(t)$ we have

$$-\infty = \liminf_{t\to\infty}(\eta_j)_{k(j)}(t) < \limsup_{t\to\infty}(\eta_j)_{k(j)}(t) = +\infty.$$

Consequently, returning to the nonlinear case through homeomorphisms g_j, a linear solution corresponds to a nonlinear bounded one $x(t)$, which satisfies, for at least one component i, the following inequality:

$$\liminf_{t\to\infty} x_i(t) < \limsup_{t\to\infty} x_i(t).$$

This concludes the proof. □

Finally, it is worth noting that Yakubovich's theorem presents some limitations in not establishing neitheir the nature of oscillations (periodic or chaotic) nor an upper and a lower bound to the oscillations.

Hopf bifurcation

First of all, let us give a preliminar definition:

Definition .4 (Equivalence of dynamical systems)**.**
A dynamical system $\frac{dx}{dt} = f(x)$, with $x(t) \in \mathbb{R}^n$ and f smooth, is topologically equivalent to a dynamical system $\frac{dy}{dt} = g(y)$, with $y(t) \in \mathbb{R}^n$ and g smooth, if there is a homeomorphism $h : \mathbb{R}^n \to \mathbb{R}^n$ mapping orbits of the first system onto orbits of the second system, preserving the direction of time.
If h is a diffeomorphism, the systems are diffeomorphic.

Consider now a dynamical system which depends on a parameter $k \in \mathbb{R}$:

$$\frac{dx}{dt} = f(x, k) \tag{15}$$

with $x(t) \in \mathbb{R}^n$ and f smooth.
As the parameter k varies, the phase portrait also might transform. There are two possibilities: either the system remains topologically equivalent to the original one or its topology changes.

Definition .5 (Parameter of bifurcation)**.**
The appearance of a topologically nonequivalent phase portrait under variation of the parameter is called a bifurcation.

Thus, a bifurcation is a change of the topology of the system as its parameter pass through a bifurcation (critical) value k_0.

There are different kinds of bifurcation. This Appendix focuses on Hopf bifurcation (also sometimes called Poincaré-Andronov-Hopf bifurcation).
This bifurcation refers to the local birth or death of a periodic solution from an equilibrium x_0 of system (15) as the parameter k crosses a critical value k_0.
It is the simplest bifurcation not just involving equilibria and it is a local one, since it can be detected only by looking at small neighborhoods of equilibria.

A Hopf bifurcation typically occurs when a complex conjugate pair of eigenvalues of the linearized flow at an equilibrium point becomes purely imaginary as the parameter k reaches a critical value k_0.
There are two types of Hopf bifurcation:
1. Hopf bifurcation in system (15) is called supercritical if the cycle exists for values of the parameter such that $k > k_0$ ("after" the bifurcation).
2. Hopf bifurcation in system (15) is called subcritical if the cycle is present "before" the bifurcation.
It seems clear what we want to say, even if the terminology used is somehow misleading, since "after" and "before" depend on the chosen direction of parameter variation.
In both cases we have a loss of stability of the equilibrium at $k = k_0$ under increase of the parameter. In the first case the stability of equilibrium x_0 is replaced by a stable limit cycle of small amplitude. Therefore, the system "remains" in a neigborhood of the equilibrium and we have a "soft" or "non-catastrophic" stability loss. In the second case the region of attraction of the equilibrium point x_0 is bounded by the unstable cycle, which shrinks as the parameter k approaches its critical value k_0 where it disappears. Thus, the system is "pushed out" from a neigborhood of the equilibrium, giving us a "sharp" or "catastrophic" loss of stability.

Let us give a theorem about Hopf bifurcation existence (see theorem 11.12 of chapter 11 of book [13]).

Theorem .8 (Poincaré-Andronov-Hopf bifurcation)**.**
Let be $\frac{dx}{dt} = f(x,k)$, with $x(t) \in \mathbb{R}^n$, $n \geq 2$, and f smooth, a dynamical system depending on a scalar parameter k.
Let be $(x_0, k_0) \in \mathbb{R}^n \times \mathbb{R}$ a couple such that

1. $f(x_0, k_0) = 0$;

2. the Jacobian matrix at x_0, $J_{|x_0}(k) = \frac{\partial f}{\partial x}(x_0, k)$, has eigenvalues

$$\lambda_{1,2}(k) = \alpha(k) \pm i\beta(k)$$

with $\alpha(k_0) = 0, \beta(k_0) \neq 0$, and, at $k = k_0$, it has no other eigenvalues with real part equal to zero;

3. the eigenvalues $\lambda_{1,2}(k)$ cross the imaginary axis with nonzero speed, that is

$$\left[\frac{dRe(\lambda_{1,2}(k))}{dk}\right]_{|k=k_0} = \left[\frac{d\alpha(k)}{dk}\right]_{|k=k_0} \neq 0.$$

Then, in x_0, for $k = k_0$, a periodic orbit (a cycle) arises with initial amplitude equal to zero and period equal to $\frac{2\pi}{\beta(k_0)}$.

Therefore, k is a Hopf bifurcation parameter around the equilibrium point x_0 and k_0 is a critical value.

Finally, let us report an example.

Example.
Consider the following planar dynamical system

$$\begin{cases} x_1' = kx_1 + x_2 - x_1(x_1^2 + x_2^2) \\ x_2' = kx_2 - x_1 - x_2(x_1^2 + x_2^2), \end{cases} \tag{16}$$

with $k \in \mathbb{R}$.
Let us take the couple $(x_0, k_0) = ((0,0), 0) \in \mathbb{R}^2 \times \mathbb{R}$.

$$f(x,k) = (f_1(x,k), f_2(x,k)) = (kx_1 + x_2 - x_1(x_1^2 + x_2^2), kx_2 - x_1 - x_2(x_1^2 + x_2^2)).$$

Clearly, $f((0,0),0) = 0$.
The Jacobian matrix at $x_0 = (0,0)$ is

$$J_{|x_0=(0,0)}(k) = \begin{pmatrix} \frac{\partial f_1}{\partial x_1} & \frac{\partial f_1}{\partial x_2} \\ \frac{\partial f_2}{\partial x_1} & \frac{\partial f_2}{\partial x_2} \end{pmatrix}_{|x_0=(0,0)} = \begin{pmatrix} k & 1 \\ -1 & k \end{pmatrix},$$

which admits the following eigenvalues:

$$\lambda_{1,2}(k) = k \pm i.$$

Then, $\alpha(0) = 0$ and $\beta(0) = 1 \neq 0$.
Finally,

$$\left[\frac{d\alpha(k)}{dk}\right]_{|k=0} = 1 \neq 0.$$

Therefore, for theorem (.10), at the origin, for $k = 0$, a periodic orbit arises with initial amplitude equal to zero and period equal to 2π.
Therefore, k is a Hopf bifurcation parameter around the origin and $k = 0$ is a critical value.
Furthermore, looking at the eigenvalues $\lambda_{1,2}(k) = k \pm i$, we can see that if $k < 0$ the origin is a stable equilibrium, while for any $k > 0$, the origin is unstable and the system admits a stable cycle of radius $\sqrt{k}$.
Consequently, since the bifurcation curve emanates from the origin to the right, the bifurcation is supercritical.

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